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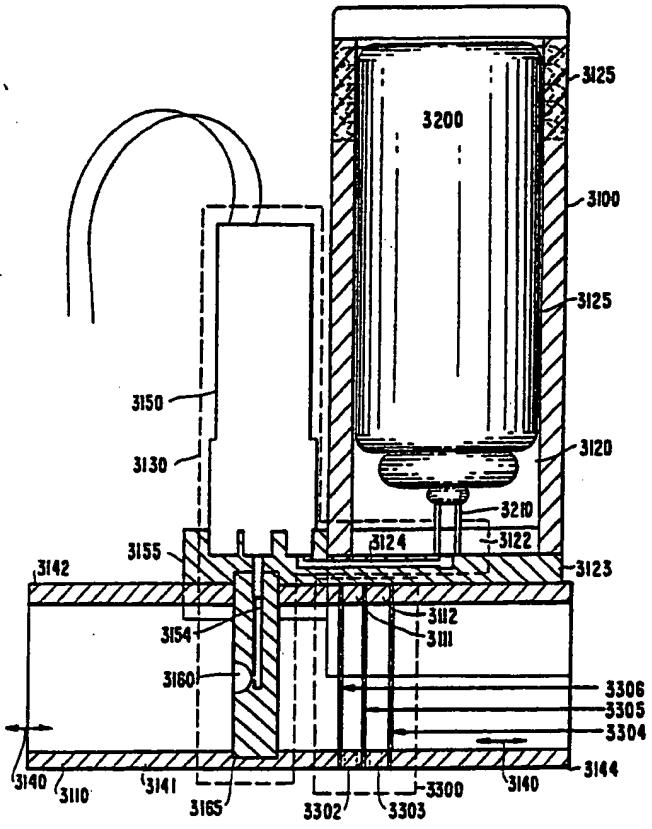
(54) Title: DELIVERY OF AEROSOL MEDICATIONS FOR INSPIRATION

(57) Abstract

Apparatus and methods for delivering an amount of aerosolized medicine for inspiration by a patient in response to the occurrence of appropriate delivery point or points in the patient's detected breath flow. The aerosol medication may be administered as one or more pulses having a pulse width, shape, and frequency that will maximize the respirable fraction of the aerosolized compound being administered. The delivery point or points may be predetermined or determined from a prior inspiratory flow for depositing the selected medication at one or more desired locations in the patient's airway. Determined delivery points are recursively lowered for each inspiratory flow that does not satisfy one of the predetermined and previously lowered thresholds. Changes in the patient's breath flow patterns during the course of an aerosolized medication inspiration therapy program may be detected and used to adjust the controlled amount of medication to be delivered in a given administration and/or to inform the patient of the patient's condition or change in condition.



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DELIVERY OF AEROSOL MEDICATIONS FOR INSPIRATION

This invention relates to improvements in the delivery of aerosolized compounds and medications for inspiration by patients.

Background of the Invention

Known devices for delivering aerosol medication for inhalation by a patient include metered dose inhalers that are manually operated and breath actuated. Breath actuated inhalers typically provide a metered dose automatically when the patient's inspiratory effort either moves a mechanical lever or the detected flow rises above a preset threshold, as detected by a hot wire anemometer. See, for example, U.S. Patents 3,187,748; 3,565,070; 3,814,297; 3,826,413; 4,592,348; 4,648,393; 4,803,978; 4,896,832; and a product available from 3M Healthcare known as Aerosol Sheathed Actuator and Cap.

A major problem with manual metered dose inhalers is that the patient frequently actuates the device at the incorrect time during inspiratory flow to obtain the benefits of the intended drug therapy or during expiration. Thus, patients may inspire too little medication, or take a second dose and receive too much medication.

One problem with breath activated drug delivery is that the dose is triggered on crossing a fixed threshold inspiratory effort. Thus, an inspiration effort may be sufficient to release a metered dose, but the inspiratory flow following the release may not be sufficient to cause the aerosol medication to pass into the desired portion of

the patient's airways. Another problem exists with patients whose inspiratory effort is not be sufficient to rise above the threshold to trigger the release valve at all.

Attempts have been made to solve the patient inspiration synchronization problem. U.S. Patent 4,484,577 refers to using a bidirectional reed whistle to indicate to the patient the maximum rate of inhalation for desired delivery of the drug and flow restrictor to prevent the patient from inhaling too rapidly. U.S. Patent 3,991,304 refers to using biofeedback techniques to train the patient to adopt a desired breathing pattern. U.S. Patent 4,677,975 refers to using audible signals and preselected time delays gated on the detection of inspiratory flow to indicate to the patient when to inspire and expire, and delivering inhalable material a selected time after the detected onset of flow. However, these devices also suffer from improper operation by patients who are not properly trained or do not conform their breathing to the instructed breathing pattern and whose inspiratory flow does not provide adequate delivery of the medication.

Studies in Byron (ed.), Respiratory Drug Delivery, CRC Press, Inc. (1990); Newman et al., Thorax 1981, 36:52-55; Newman et al. Thorax, 1980, 35:234; Newman et al., Eur. J. Respir. Dis., 1981, 62:3-21; and Newman et al., Am. Rev. Respir. Dis., 1981, 124:317-320 indicate that during a single breath of an aerosol compound, only about ten percent of the total aerosol material presented is deposited into the lungs and that the location of deposition in the lung depends upon 1) breath parameters such as volume of inspiration, inspiratory flow rate, inspiratory pause prior to expiration, the lung volume at the time the bolus of medication is administered, and expiratory flow rate, 2) the size, shape and density of the aerosol particles (i.e., the medicinal compound, any carrier, and propellant), and 3) the physiological characteristics of the patient.

Byron reports that two peak deposition fractions occur. One is in the larger airways where airways velocity is

highest and inertial impact is maximal. This effect is not seen in medium sized airways where velocity is lower and airway size is too large to permit deposition by sedimentation under gravity. The second peak deposition fraction appears in the more distal and smaller airways where velocity is slowest and deposition by sedimentation occurs.

The Newman references refer to measuring inspired air with a pneumotachograph to obtain a flow rate signal, which is integrated by a computer to determine lung capacity. A determined lung capacity, as a percent of vital capacity, is used as a threshold to actuate a solenoid to depress the canister of a manually actuated metered dose inhaler on the inspiration of the predetermined lung volume.

A problem with existing metered dose inhalers, whether or not breath actuated, is that they are factory preset to deliver a fixed dose at a given particle size distribution. Thus, those devices are not capable of reducing the dose to reflect improvement in the patient's condition, or selecting a maximum desired respirable fraction of the aerosol mist that is suitable for a desired location of delivery of the medication in the particular patient.

Devices for controlling particle size of an aerosol are known. U.S. Patent 4,790,305 refers to controlling the particle size of a metered dose of aerosol for delivery to the walls of small bronchi and bronchioles by filling a first chamber with medication and a second chamber with air such that the all of the air is inhaled prior to the inhaling medication, and using flow control orifices to control the flow rate. U.S. Patent 4,926,852 refers to metering a dose of medication into a flow-through chamber that has orifices to limit the flow rate to control particle size. U.S. Patent 4,677,975 refers to a nebulizer device that uses baffles to remove from an aerosol particles above a selected size. U.S. Patent 3,658,059 refers to a baffle that changes the size of an aperture in the passage of the suspension being inhaled to select the quantity and size of

suspended particles delivered. A problem with these devices is that they process the aerosol after it is generated and thus are inefficient and wasteful.

If is well known that pulmonary functions, such as forced expiratory volume in one second, forced vital capacity, and peak expiratory flow rate, can be measured based on measured flow rates and used both to diagnose the existence of medical conditions, to prescribe medication, and to ascertain the efficiency of a drug therapy program. See for example, U.S. Patents 3,991,304 and 4,852,582 and the Newman references discussed above. Heretofore, these tests have been performed using available spirometers. U.S. Patent 4,852,582 also refers to using a peak flow rate meter to measure changes in peak flow rate before and after administration of a bronchodilator. The results of such tests before and after administration of several different medications are used to evaluate the efficiency of the medications.

A problem with the foregoing pulmonary function test devices is that they are complicated for most patients to perform. Another problem is that the test data must be examined and interpreted by a trained medical practitioner to be meaningful. Another problem is that they do not provide adequately for altering the dosage of the medication administered in a single patient during the course of therapy, or from patient to patient, using the same delivery device for generating an aerosol of the same or different medications.

Summary of the Invention

It is, therefore, an object of this invention to provide improved apparatus, systems, and methods for delivering aerosol compounds for inspiration by a patient.

It is another object of this invention to provide improved apparatus, systems, and methods for delivering for inspiration an aerosol having a particle size distribution favorable for selective deposition into desired locations in

a patient's pulmonary system. It is another object to release a controlled amount of aerosol in one or more pulses having a selected pulse size, shape, and frequency and number of pulses to produce a selected particle size distribution. It is another object to provide a variably actuated valve mechanism having an open state and a closed state for controlling the medication pulse size, shape, and frequency, to produce a pulse train having a selected particle size distribution at a selected point or a series of selected points in the patient's inspiratory flow and, further, to produce a pulse train so that the particle size distribution delivered at different points in the flow may be different.

It is another object of the invention to deliver aerosolized compounds in response to a measure of a patient's breathing pattern during inspiration. It is another object to select the optimal point or points for release of one or more pulses of medication based on an analysis of the patient's inspiratory flow in a first detected flow and to release the medication on the occurrence of the determined point or points during a subsequently detected inspiratory breath.

It is another object to select the location of deposition of the medication in the patient's airway by selecting the optimal point or points in the inspiratory flow to achieve such deposition. It is another object to deposit selectively the medication based on a selected optimal flow point and a selected pulse train to obtain a desired respirable fraction for such deposition. It is another object to prompt the patient to hold his or her breath for an optimal period of time at the end of inspiration to optimize delivery of the aerosolized compound being administered.

It is another object of the invention to release automatically a controlled amount of medication when the patient's detected inspiratory flow exceeds a preselected or default delivery threshold, and, if the first detected flow

does not exceed (or satisfy) the default delivery threshold, to determine a new delivery threshold based on a detected flow maxima parameter of the previously detected inspiratory flow not exceeding the prior delivery threshold and to release a controlled amount of medication when a subsequently detected flow exceeds the new determined delivery threshold. The determined threshold is thus recursively determined for each detected inspiratory flow not exceeding the previously established delivery threshold, whether that threshold is the preselected default triggering threshold or a subsequently determined threshold.

It is another object of this invention to provide improved apparatus, systems, and methods for delivering aerosolized compounds for inspiration by a patient by incorporating a measure of a patient's pulmonary function to provide for varying the dosage or controlled amount of the aerosolized compound delivered for inspiration by the patient in response to detected changes in the patient's pulmonary function during a course of therapy directed to improving pulmonary function.

It is another object to provide improved apparatus, systems, and methods for delivering aerosol compounds for inspiration by a patient by incorporating a measure of a patient's pulmonary function and an acuity display of that function to the patient, for example, to provide for alerting the patient whether the patient's determined function indicates whether the patient should continue the inhalation drug therapy program or seek immediate medical attention.

It is another object of the present invention to provide a programmable, durable variable dose inhaler whereby the medication being administered can be selected and the inhaler can be programmed to provide for efficacious delivery of the selected medication to a given patient. It is another object to provide an improved inhaler with audible, visual or audiovisual feedback for prompting the patient to obtain a suitable breathing pattern for

delivering a selected medication at an appropriate time based on the patient's detected inspiratory flow and, optionally, for measuring a pulmonary function. It is another object to provide feedback for prompting the patient's breathing pattern in response to previously measured pulmonary or flow parameters for automatic administration of the selected medication. It is another object to provide a visual display of the adequacy of a dosage delivered and other parameters regarding the course of therapy, such as time of next dose to be administered. It is another object to provide the medical examiner with a history log of drug administration and points of drug delivery for evaluation.

A further object of the present invention is to provide a hand held microprocessor controlled inhaler device for use in outpatient aerosol drug therapy that is capable of autonomously modifying the initial therapy program based on detected progressive changes in the patient's breath flow and corresponding pulmonary functions. It is another object to provide for communications between the device and a remote station for remote reprogramming of the microprocessor controlled device for external modification of the therapy or for transmitting historical log data for evaluation.

It is another object to provide a disposable mouthpiece containing a nozzle for dispensing medication and a flow rate sensor located in the flow path to detect flow so that it does not interfere with generation of an aerosol for inspiration by a patient.

The present invention increases the effectiveness and utility of devices for delivering aerosolized medications and overcomes the problems of the prior known devices. Broadly, the invention concerns methods and apparatus for achieving the above objectives based on detecting the patient's inspiratory flow and releasing one or more pulses of an aerosol medication respectively at one

or more identified points in the detected flow to provide an efficacious delivery of a selected amount of medication.

The following terms are used in describing the present invention. The term "delivery point" refers to a point in the detected inspiratory flow at which an amount of aerosol is to be delivered. The term "amount of aerosol" refers to the amount released in response to the occurrence of a delivery point. The amount may be either a single pulse, or a preselected number of pulses, e.g., four pulses having the same shape and frequency. The term "delivery schedule" refers to one or more delivery points in the detected inspiratory flow. A full dosage of aerosol is delivered in accordance with the delivery schedule. Thus, a delivery schedule that includes only one delivery point will deliver the amount of aerosol in response to the occurrence of that point in the detected inspiratory flow. A delivery schedule that includes more than one delivery point will deliver an amount of aerosol in response to the occurrence of each point in the delivery schedule in the detected inspiratory flow such that the sum of the aerosol amounts totals the full dosage. The term "delivery threshold" refers to the first delivery point in the delivery schedule. If a detected inspiratory flow satisfies the delivery threshold, the event is considered to be a successful delivery of aerosol, whether or not any subsequent delivery points in the delivery schedule are satisfied and a full dosage is delivered. The term "flow" refers to one of a flow rate in volume per time, a flow volume (which may be calculated from the time integral of the determined flow rate), and a combination of flow rate and flow volume.

One aspect of the invention concerns an oral drug delivery device that delivers each dosage as a sequence of pulses selected to increase the effective respirable fraction of medication delivered compared to a conventional metered dose inhaler device. More particularly, each pulse is provided with a selected pulse width, shape, and frequency that will maximize the respirable fraction of the

aerosolized compound being delivered. This pulse selection also will allow manipulation of the cumulative particle size distribution so as to enhance delivery of the aerosolized compound to desired loci in the airway.

One preferred embodiment of this aspect of the invention is directed toward an apparatus for controlling the particle size distribution to maximize the respirable fraction of an aerosol. One such device includes:

(a) a source of aerosol generating material;

(b) a valve, associated with the source, having a first state for releasing an amount of aerosol generating material and a second state for not releasing an amount of aerosol generating material;

(c) means for selecting the relative time the valve is in the first state and the second state to maximize respirable fraction of an aerosol pulse, the valve being in the first state for a time selected from between about 10 to about 1000 msecs; and

(d) means for cycling the valve between states in response to the selected relative time to release an amount of aerosol having the maximized respirable fraction, wherein the valve is cycled at a rate at or below 100 cycles per second.

Another preferred embodiment of this aspect of the invention concerns a method for controlling the respirable fraction of an aerosol in an aerosol drug delivery device having a source of aerosol generating material and a valve having a first state for releasing an amount of aerosol generating material and a second state for not releasing an amount of aerosol generating material. One such method includes:

(a) selecting the relative time the valve is in the first state and the second state to select the maximum respirable fraction of an aerosol pulse, the valve being in the first state for a time selected from between about 10 to about 1000 msecs; and

(b) cycling the valve from the second state to the first state to the second state in response to the selected relative time to release an amount of aerosol having the maximized respirable fraction, the cycling occurring at a rate at or below 100 cycles per second.

The time the valve is opened in the first state is selected to produce a mist having a cumulative particle size distribution selectively favoring small or large particles as desired. The time open is preferably between 10 and 1000 msec. The valve may be operated asynchronously or synchronously to produce one or more pulses such that each full dosage of aerosol includes one pulse or more than one pulse of non-uniform or uniform pulse widths, shapes, and intervals between pulses. Preferably, the valve is cycled in response to a detected inspiratory flow satisfying a provided delivery schedule. Further, the pulses may be provided with selected particle size distributions that vary from pulse to pulse whether in response to the same or different delivery points.

In a preferred embodiment, the valve and the operating valve means are an electromechanically controlled valve actuator, such as an integral solenoid and valve. The integral solenoid and valve device is preferably interposed in a flow channel from the source of aerosol generating material to a nozzle that produces the aerosol. It can be used to meter the contents of a pressurized canister to provide an aerosol pulse train having, for example, synchronous pulses of uniform size, asynchronous pulses of uniform size, synchronous pulses of non-uniform size, asynchronous pulses of non-uniform size, and combinations thereof. Preferably, a series of four pulses having a duty cycle of from 8 to 15% are used to deliver an amount of aerosol in response to each delivery point in a delivery schedule satisfied by the flow. Thus, the delivery schedule provided may be selected so that the given respirable fraction of the one or more pulses will be deposited in a desired location in the patient's airways. In this regard, particles intended for deep airway deposition would be delivered in the inspiratory flow earlier, or at relatively lower flow rates and volumes, than particles intended for deposition in peripheral airways.

Another aspect of the present invention concerns an apparatus for selecting the delivery schedule based on the patient's measured inspiratory flow.

In a preferred embodiment, the apparatus has a preprogrammed, default delivery schedule whereby if the patient's first detected inspiratory flow does not satisfy the first delivery point, namely, the delivery threshold, the apparatus enters a calibration mode. The delivery schedule is further selected for depositing the particles in the desired location for efficacious treatment of the patient. The term "first detected inspiratory flow" refers to the first inspiratory flow detected subsequent to a selected reset flow event, for example, the apparatus being turned on, the device being reset, a successful delivery of an aerosol and the expiration of a selected time interval without delivery of an aerosol.

In the calibration mode, the apparatus selects a new delivery schedule based on the preceding inspiratory flow (which failed to satisfy its delivery threshold), prompts the patient to take another breath, and, on satisfaction of the newly selected delivery threshold during the subsequently detected inspiratory flow, delivers the aerosol in accordance with the delivery schedule to the extent that any subsequent delivery points are satisfied by the detected inspiratory flow. Thus, the patient receives the selected aerosol medication at the determined optimal delivery point or points for depositing the administered aerosolized compound at preferred loci in the lung.

Once in the calibration mode, if a subsequent breath does not satisfy the newly determined delivery threshold, a recursive routine is used for selecting a new delivery threshold for each successive inspiratory effort that does not satisfy a determined point threshold which results in successively lowering the delivery threshold by a predetermined amount. The predetermined amount is preferably a sequence of predetermined percentages of the measured flow of the preceding inadequate breath. For

delivery schedules having more than one delivery point, typically all delivery points will be lowered by the same percentage as the threshold point. Thus, the device is configured to deliver eventually medication to the patient taking into consideration the patient's inspiratory abilities at the time of dosage administration and the aerosol medication to be delivered. The delivery threshold may be based on an inspiratory flow rate, more particularly, a selected rate prior to the occurrence of the peak inspiratory flow rate, e.g., for a preselected threshold a rate in the range of 20 to 30 liters per minute, an inspiratory flow volume, e.g., for a preselected threshold a volume of about 1.0 liter. More preferably, the delivery threshold is a combination of a flow rate and a flow volume as a pair. Preferably, once a delivery of aerosol is made, the apparatus will return to its preprogrammed default operating mode and preselected delivery schedule whether or not the full dosage of aerosol has been administered.

One preferred embodiment of this aspect of the invention is directed towards an apparatus for delivering an aerosol from a supply of aerosol generating material for inspiration by a person in response to the detected inspiratory flow of the person. One such apparatus includes:

a valve in communication with the supply of aerosol generating material;

means for operating the valve to release an amount of aerosol generating material to form an aerosol;

means for detecting an inspiratory flow of the person;

means for controlling the valve operating means in response to the detected inspiratory flow comprising:

first means for determining whether each detected inspiratory flow is one of a first flow or a subsequent flow, the first flow corresponding to one of the first attempt to deliver an amount of aerosol and the first attempt to deliver an amount of aerosol following delivery of an amount of aerosol, the subsequent flow corresponding to an

inspiratory flow detected subsequent to a preceding detected inspiratory flow not followed by delivery of an amount of aerosol;

means for providing a delivery threshold corresponding to a point in the detected inspiratory flow at which an amount of aerosol is to be delivered, the provided delivery threshold being a preselected delivery threshold in response to the detected inspiratory flow being determined to be a first flow, and a determined delivery threshold in response to the detected inspiratory flow being determined to be a subsequent flow, the providing means including means for calculating the determined delivery threshold based on the preceding detected inspiratory flow; and

second means for determining whether or not the detected inspiratory flow satisfies the provided delivery threshold so that the controlling means operates the valve to deliver an amount of aerosol in response to the second determining means determining that the detected inspiratory flow satisfies the provided delivery threshold.

Another aspect of this embodiment of the invention is directed toward a method of delivering an aerosol to a person for inspiration using a device having a supply of aerosol generating material and a valve for releasing an amount of aerosol generating material to form an aerosol, and a means for detecting inspiratory flow of the person. One such method includes the steps of:

(a) detecting an inspiratory flow of the person;

(b) determining whether each detected inspiratory flow is one of a first flow or a subsequent flow, the first flow corresponding to one of the first attempt to deliver an amount of aerosol and the first attempt to deliver an amount of aerosol following delivery of an amount of aerosol, the subsequent flow corresponding to an inspiratory flow detected subsequent to a preceding detected inspiratory flow not followed by delivery of an amount of aerosol;

(c) selecting a delivery threshold corresponding to a point in the detected inspiratory flow at which an amount of aerosol is to be delivered so that a preselected delivery threshold is selected in response to determining that the detected inspiratory flow is a first flow, and a determined delivery threshold is selected in

response to determining that the detected inspiratory flow is a subsequent flow; and

(d) determining whether or not the detected inspiratory flow satisfies the selected delivery threshold; and

(i) in response to the detected inspiratory flow satisfying the selected delivery threshold, operating the valve to release an amount of aerosol generating material to form an aerosol; or

(ii) in response to determining that the detected inspiratory flow did not satisfy the selected delivery threshold, calculating a new delivery threshold based on the detected inspiratory flow so that the selected delivery threshold for the next detected inspiratory flow determined to be a subsequent flow is the calculated delivery threshold.

In a preferred embodiment of this aspect of the invention, the calculating means and method step for providing the determined delivery threshold determines the delivery threshold based on the detection of an inspiratory flow not satisfying the provided delivery threshold, and can recursively determine new delivery thresholds for each successive detected inspiratory flow that fails to satisfy each provided delivery threshold, notwithstanding that the delivery thresholds are successively lowered. One such calculating means includes:

means for measuring a selected flow parameter of the detected inspiratory flow in response to second determining means determining that the detected inspiratory flow did not satisfy the provided delivery threshold; and

means for adjusting the provided delivery threshold in response to the measured flow parameter, thereby providing the determined delivery threshold.

One method includes measuring a selected flow parameter of the detected inspiratory flow in response to determining that the detected inspiratory flow did not satisfy the selected delivery threshold and adjusting the selected delivery threshold in response to the measured flow parameter. The selected flow parameter may be a point

corresponding to the detected maxima of flow rate, flow volume, or some combination of flow rate and flow volume, such that the adjustment is a percentage of the detected flow parameter.

Preferably, the delivery threshold further comprises a delivery schedule including the delivery threshold as the first delivery point and one or more additional delivery points in the detected flow following the delivery threshold, such that an amount of aerosol is to be delivered at each delivery point in the schedule. Also, for detected inspiratory flows that are determined to be subsequent flows, adjusting the delivery schedule adjusts every point in the delivery schedule and determining whether or not the detected inspiratory flow satisfies the delivery threshold also determines whether or not each delivery point in the delivery schedule is satisfied so that an amount of aerosol is delivered for each delivery point in the delivery schedule that is satisfied by the detected inspiratory flow.

In an alternate embodiment of this aspect of the invention, concerning selecting the delivery schedule based on the person's measured inspiratory flow, the apparatus is configured to operate in a mode whereby a first inspiratory flow is detected, a delivery schedule corresponding to the optimal delivery threshold (and optionally additional delivery points) for the administration of the selected aerosol medication is determined based on a measure of the detected inspiratory flow parameters, and a subsequently detected inspiratory flow is detected and compared to the delivery schedule whereby an amount of aerosol will be delivered in accordance with the delivery schedule upon satisfaction of each delivery point in the determined delivery schedule by the subsequently detected inspiratory flow.

One such apparatus includes:

(a) a reservoir containing an aerosol generating material;

(b) valve means for releasing an amount of the aerosol generating material from the reservoir, thereby to form an aerosol;

(c) means for detecting an inspiratory flow of the person including a first inspiratory flow and a second inspiratory flow occurring subsequent to the first inspiratory flow;

(d) first means for evaluating the first detected inspiratory flow to identify an appropriate delivery threshold for the delivery of an aerosol;

(e) second means for evaluating the second detected inspiratory flow and determining whether the second detected flow satisfies the determined delivery threshold; and

(f) means for actuating the valve means in response to the second detected inspiratory flow satisfying the delivery threshold, thereby to deliver an amount of aerosol during the second detected inspiratory flow.

Another aspect of this alternate embodiment of the invention is directed to a method of administering a controlled amount of medication using a device having a supply of aerosol generating material and a valve for releasing an amount of aerosol generating material to form an aerosol and a means for detecting an inspiratory flow of a person. One such method includes the steps of:

(a) detecting a first inspiratory flow of the person;

(b) determining a delivery threshold for the delivery of an amount of aerosol based on the first detected inspiratory flow;

(c) detecting a second inspiratory flow of the person;

(d) determining whether or not the detected second inspiratory flow satisfies the determined delivery threshold; and

(e) operating the valve to deliver the amount of aerosol in response to determining that the second inspiratory flow satisfies the determined delivery threshold.

Preferably, in the apparatus and methods of this alternate embodiment, for each second inspiratory flow that

does not satisfy a determined delivery threshold, the second inspiratory flow is treated as the first inspiratory flow such that the first determining means determines a new delivery threshold (or delivery schedule) based on the evaluation of that detected inspiratory flow. Another inspiratory flow is then detected (the third) and treated as the second detected inspiratory flow. Thus, the second determining means evaluates the latter (third) flow and determines whether it satisfies the determined delivery threshold based on the preceding (second) flow. The apparatus will continue to determine a new delivery threshold based on a selected detected inspiratory flow, which threshold is used for a following detected inspiratory flow. In this manner, the apparatus will eventually deliver an amount of aerosol medication to the person, even in the event of a degrading inspiratory flow effort. In other respects, this alternate embodiment is similar in operation to the previously described embodiment.

In either embodiment the dosage of aerosol medication may be adjusted over time based on measured changes in the patient's pulmonary functions and, further, each dosage is released based on a delivery schedule, either determined, preprogrammed or recursively determined, so that the administration of aerosol medication occurs automatically in accordance with a desirable delivery schedule in the patient's detected inspiratory flow and with a particle size distribution to maximize the efficacy of the medication.

In either embodiment of this aspect of the invention, the means for detecting the inspiratory flow is preferably a tube defining an inspiratory flow path having a mouth end and an open end and a flow transducer disposed in the flow path. The flow transducer may be selected from among a flow resistive device or structure which generates a pressure drop across the device (referred to as a differential pressure transducer or structure) and an associated means for converting the measured differential

pressure into an inspiratory flow rate, e.g., a pneumotach, a hot wire anemometer and means for converting the measured temperature changes into an inspiratory flow rate, and similar devices for providing a flow rate signal.

Preferably, the inspiratory flow path includes a means for providing a laminar flow through the inspiratory flow path so that the flow transducer detects the differential pressure across a laminar air flow. The laminar flow provides a flow and a flow path having linear characteristics for converting the differential pressures to flow rate. In embodiments not having a laminar flow means or using structures, transducers and/or inspiratory flow paths not having such linear flow characteristics, such as venturi ports or a single resistive flow screen, the flow path may be encoded by an array of predetermined calibration constants such that nonlinear characteristics of the differential pressures detected across the flow resistive device may be converted by use of the calibration constant array for the range of pressures detected to flow rates, directly or indirectly. Preferably, a differential pressure transducer for use in the present invention will have a differential pressure sensitivity in the range of ±25.4 cm of water corresponding to a flow rate of from about 0 to about 800 liters per minute.

Another aspect of the invention concerns methods and apparatus for monitoring the patient's breath flow patterns during the course of an aerosolized medication inspiration therapy program and determining the patient's pulmonary function based on detected flow. In one embodiment, a display device is provided for displaying the patient's determined pulmonary function. The display device may be used to indicate the patient's instantaneous condition when an instantaneous pulmonary function is measured. The display device also may be used to indicate relative changes in condition when a subsequent measure of the pulmonary function is compared to a prior measure (or to a historical average of the measures, e.g., a weighted average) of that

pulmonary function. Importantly, this display will indicate to the patient when measured functions indicate that the patient should seek medical attention. Thus, the present invention is believed to overcome the problem of patients not knowing whether their medical condition is better, worse or unchanged, or is being adequately treated during the course of medication.

In another embodiment, the relative changes in measured pulmonary function may be used to adjust the dosage of medication based on the determined changes in the determined function. This may occur based on a relative change determined from one administration of medication to the next, or from a baseline measured pulmonary function (or a weighted average historical record) to the next administration of medication. In addition, the patient's pulmonary condition may be displayed. Thus, this aspect of the present invention provides for optimizing the effectiveness of the medication within the limits of preselected parameters, considering such things as maximum allowable dosages for the given patient and the frequency of medication.

One embodiment of this aspect of the invention is directed towards an apparatus and method for measuring the patient's pulmonary function and displaying a visual acuity of the measured function to the patient. One such apparatus includes

means for detecting a breath parameter of the person selected from among one or more of inspiratory flow and expiratory flow;

means for determining a pulmonary function of the person based on a measure of at least one of the detected breath parameters;

a first visual indicator corresponding to a first range of pulmonary conditions for the determined pulmonary function; and

a second visual indicator corresponding to a second range of pulmonary conditions for the determined pulmonary function, the first and second ranges being contiguous;

means for evaluating the determined pulmonary function and illuminating the one of the first and second visual indicators whose corresponding range includes the determined pulmonary function.

More than one visual indicator may be used, more preferably three visual indicators corresponding to three contiguous ranges of acceptable condition, marginal condition, and unacceptable condition.

In a preferred embodiment, the apparatus of this aspect of the invention may be configured to acquire a second measure of pulmonary function, compare that measure to a prior measure, and display trend data to the patient, thereby to indicate whether the person's medical condition is improving, degrading, or remaining about the same. One such apparatus includes:

means for comparing a first determined pulmonary function to a second determined pulmonary function and indicating whether or not the patient's determined pulmonary function has changed from the first to the second determinations, the first determined pulmonary function being based on a first detected breath parameter and the second determined pulmonary function being based on a second detected breath parameter subsequent to the first detected breath parameter; and

means for displaying whether the detected pulmonary function has improved on a first visual indicator, remained nominally the same on a second visual indicator, and degenerated on a third visual indicator in response to the indicated change in the first and second determined pulmonary functions.

One method of this aspect of the invention includes the steps of:

(a) detecting a breath parameter of the person selected from among one or more of an inspiratory flow and an expiratory flow;

(b) determining a pulmonary function of the person based on a measure of at least one of the detected breath parameters;

(c) selecting a first range of pulmonary conditions for the determined pulmonary function and a second range of pulmonary conditions for the determined

pulmonary functions, the first and second ranges being contiguous;

(d) providing a first visual indicator corresponding to the first selected range and providing a second visual indicator corresponding to the second selected range;

(e) evaluating the determined pulmonary function with respect to the first and second selected ranges and identifying which range includes the determined pulmonary function; and

(f) illuminating the visual indicator corresponding to the identified selected range including the determined pulmonary function.

Preferably, the method includes providing more than two contiguous ranges of pulmonary conditions and more than two corresponding visual indicators for each selected range so that, for example, the measured pulmonary function can be compared to ranges of nominal, marginal, and unacceptable ranges of pulmonary conditions, and the visual indicator corresponding to the selected range including measured pulmonary function can be illuminated.

In an alternate embodiment of the above method, the method includes acquiring a second breath parameter subsequent to the previously measured pulmonary function and measuring a second pulmonary function, comparing the second measured pulmonary function to the first measured pulmonary function, indicating whether or not the patient's determined pulmonary function has changed from the first to the second determinations, providing a first, second, and third visual indicators, and displaying whether the second measured pulmonary function has improved on the first visual indicator, remained nominally the same on the second visual indicator, and degenerated on the third visual indicator, relative to the previously measured pulmonary function.

Another preferred embodiment of this aspect of the invention is directed to an apparatus for selecting the dose of aerosol medication for inspiration by a patient in

response to detected changes in pulmonary function. One such apparatus comprises:

(a) a reservoir containing an aerosol generating material including medication;

(b) means for detecting a patient's breath flow;

(c) means for calculating a pulmonary function in response to a detected breath flow;

(d) means for determining a first pulmonary function in response to a first detected breath flow;

(e) means for determining a second pulmonary function corresponding to a second detected breath flow, the second detected breath flow occurring subsequent to the first detected breath flow;

(f) means for comparing the first determined pulmonary function and the second determined pulmonary function to identify relative changes in pulmonary function over time; and

(g) means for releasing a controlled amount of medication from the reservoir in response to the first and second determined pulmonary functions so that the controlled amount is adjusted for identified relative changes in the first and second determined pulmonary functions.

Preferably, the apparatus and methods further provide means for identifying the appropriate delivery schedule in a detected inspiratory flow for releasing the dosage of aerosol medication, and means for delivering a dosage of aerosol adjusted in response to identified relative changes in the first and second pulmonary functions, a subsequently detected inspiratory flow satisfying the delivery schedule. Means for recursively adjusting the delivery schedule may be provided when a detected inspiratory flow does not satisfy a delivery threshold.

This aspect of the invention also is directed to a method for adjusting the controlled amount of medication in response to detected changes in pulmonary function over time. One such method includes the steps of:

(a) detecting a patient's first breath flow;

(b) determining a first pulmonary function in response to the detected first breath flow;

(c) detecting a patient's second breath flow subsequent to the first breath flow;

(e) determining a second pulmonary function in response to the detected second breath flow;

(f) comparing the first and second determined pulmonary functions and identifying relative changes between the first and second determined pulmonary functions; and

(g) adjusting the amount of aerosol to be delivered in response to the identified changes in pulmonary function.

It should be understood that, in the context of comparing two measured pulmonary functions, the term first breath flow or first detected pulmonary function may be one of the previously acquired measurement, a baseline measurement made at the beginning of the medication therapy, and a changing weighted average of previously acquired measurements, whereby the weights may be selected to favor more recently acquired or less recently acquired measurements. Thus, the latter acquired measurement may be compared to such a first measurement for indicating short term relative changes, absolute changes from a baseline, or more long term relative changes.

Preferably, the apparatus releases one or more pulses at the appropriate points in the patient's inspiratory flow to optimize the deposition of the administered aerosolized medication within the desired loci within the lung. The apparatus also may adjust the controlled amount of medication delivered and/or the particle size in each dosage of medication delivered in response to detected changes in the patient's pulmonary function.

Another aspect of the invention concerns a portable, hand held device for use in delivering aerosolized medications to a patient. One such apparatus includes:

a tube forming a flow path having a mouth end and an open end;

a nozzle disposed in the tube directed toward the mouth end;

a flow transducer disposed in the inspiratory flow path for detecting the patient's breath flow including an inspiratory flow;

a receptacle for receiving a supply of aerosol generating material;

an aerosol flow path extending from the receptacle to the nozzle;

a valve interposed in the aerosol flow path for opening and closing the flow path; and

means for actuating the valve to open and close the flow path for delivering an amount of aerosol out the nozzle.

In a preferred embodiment, the device further include, means for detecting the patient's inspiratory flow and operating the actuating means to deliver an amount of aerosol to the patient during the detected inspiratory flow.

Further, means for receiving a supply of power for operating the device may be disposed in the receptacle so that the receiving means can electrically connect to a source of power, e.g., a battery, associated with the supply of medication.

In another embodiment of this aspect of the invention, the valve and actuating means may be an electromechanical device, such as an integrated solenoid and valve. More preferably, the solenoid is operated to deliver the aerosol at a pulse cycle of one or more pulses to provide the aerosol with a selected particle size distribution so as to maximize the respirable fraction of the administered aerosolized compound. Also, the flow transducer is preferably a differential pressure transducer and the means for detecting the patient's inspiratory flow converts the detected differential pressures into flow measurements. In one embodiment, the flow transducer is

accompanied by a laminar flow device so that the differential pressures are directly related to measured flow. In an alternate embodiment, the flow transducer does not use a laminar air flow and the detecting means uses a set of calibration constants to convert the detected differential pressures into measured flow. It should be understood, however, that most air flow paths have some degree of non-linearity which can be corrected by use of calibration constants. A filter may be provided between the mouth end of the tube and the flow transducer to prevent particulate matter from interfering with the flow measurement or clogging the flow transducer, particularly differential flow pressure transducers.

In another embodiment of this aspect of the invention, the tube, including the flow path, the flow transducer (and any filter associated therewith), a portion of the aerosol flowpath, and the nozzle may be detachable from the other portions of the device so that it may be replaced after use. In this embodiment, the aerosol flow path may be comprised of two interconnecting channels, one extending from the receptacle to a port proximate to the tube, and the other extending from that port to the nozzle.

Brief Description of the Drawings

Further features of the invention, its nature and various advantages will be more apparent from the accompanying drawings and the following detailed description of the invention in which like reference numerals refer to like elements and in which:

FIG. 1 is a side cross sectional view of an embodiment of the present invention;

FIG. 2 is side cross sectional view of an embodiment of the present invention;

FIG. 3 is a front partial sectional view taken along line 3-3 of FIG. 1;

FIG. 4 is a schematic diagram of the digital control circuits of the device of FIG. 2B;

FIG. 5 is a schematic diagram of a reset circuit of FIG. 4;

FIG. 6 is a schematic diagram of the analog module of FIG. 4;

FIG. 7 is a schematic diagram of an LED annunciator module of FIG. 4;

FIG. 8 is a schematic diagram of an LED annunciator module of FIG.4;

FIG. 9 is a schematic diagram of an LED annunciator module of FIG. 4;

FIG. 10 is a schematic diagram of the solenoid control module of FIG. 4;

FIG. 11 is a schematic diagram of the speaker module of FIG. 4;

FIG. 12 is a flow chart of a preferred embodiment of the device of FIG. 4 in accordance with the present invention; and

FIGS. 13A-13E are collectively a flow chart of an illustrative subroutine calling chain of the software embodiment of FIG. 12.

Detailed Description of the Invention

Referring to FIGS. 1, 2, and 3, one embodiment of the present invention includes base 3100, canister 3200, flow sensor 3300, solenoid valve 3150, aerosol delivery system 3130, mouthpiece 3110, and control circuits 3400 (circuits 3400 not shown in FIG. 2). Canister 3200 preferably contains a medication under pressure and has a valve 3210 for releasing medication. Base 3100 includes a receptacle 3120 for receiving canister 3200, a valve seat 3122 for receiving canister valve 3210, and means 3125 for retaining canister 3200 in receptacle 3120 as described herein. Means 3125 is preferably a threaded cap that screws into (FIG. 2) or about (FIG. 1) the open end of receptacle 3120 so that an inserted canister 3200 is fully seated in receptacle 3120 in a stationary position. In the fully seated position, canister valve 3210 is depressed open and

the contents of canister 3200 are thus in communication with aerosol delivery system 3130.

Means 3125 may include alternate structures for locking canister 3200 in the fully seated position, for example, a locking hinged lid or a conventional bayonet mount connection wherein the canister body has one or more protrusions that mesh with one or more receptacles in receptacle 3120 when the canister is fully inserted and rotated in receptacle 3120.

Canister 3200 is preferably a conventional canister containing the medication to be delivered and a suitable propellant or carrier for the medication and having valve 3210 for controlling the release of medication when valve 3210 is depressed and thus opened. Such canisters 3200 are commercially available from a variety of sources and are well known in the art. One such canister is model No. C-128-S available from Prespart Co. and one suitable valve for that canister is a straight valve model no. BK-295, available from BESPAK, King's Lynn, England.

Aerosol delivery system 3130 operates under the control of control circuits 3400 and provides one or more pulses of medication from canister 3200 to airflow path 3140 and mouthpiece 3110 by selective control of solenoid valve 3150. System 3130 includes valve seat 3122, inlet channel 3124, solenoid valve 3150, outlet channel 3154, and aerosol nozzle 3160. Inlet channel 3124 forms a gas communication path between canister 3200 and solenoid valve 3150 for passing the pressurized contents of canister 3200 to valve 3150. Outlet channel 3154 forms a gas communication path from valve 3150 to nozzle 3160, for passing the pressurized contents of canister 3200 to nozzle 3160 to deliver an aerosol into air flow path 3140.

When solenoid valve 3150 is inactive or closed, inlet channel 3124 does not pass gas therethrough. Channel 3124 thus will equilibrate with the contents of canister 3200. Similarly, outlet channel 3154 does not pass gas therethrough and will equilibrate with the atmosphere. When

valve 3150 is actuated or open, channels 3124 and 3154 are in open communication and the contents of canister 3200 are released to the atmosphere through nozzle 3160 to form an aerosol. Solenoid valve 3150 thus controls the delivery of the contents of canister 3200 to the patient as described further herein.

Referring to FIG. 1, channel 3124 is tooled in manifold 3123 and manifold 3155, which respectively interface receptacle 3120 and solenoid 3150, and channel 3154 is tooled in manifold 3155 for interfacing solenoid 3150 and nozzle 3160. The use of manifolds provides for removable interconnections for repair, cleaning or replacement of parts of base 3100.

Air flow path 3140 is formed of a tube 3141, preferably having a flattened cylindrical cross section, and includes a mouthpiece 3110 at mouth end 3142 and flow sensor 3300 at back end 3144. Interposed between mouth end 3142 and back end 3144 is a projection 3165 which contains nozzle 3160 and is secured to the wall of air flow path 3140. Projection 3165 is provided with a dimension that does not interfere with flow through path 3140 and preferably extends diametrically across flow path 3140 so that nozzle 3160 is directed to release an aerosol into, and in longitudinal alignment with air, flow path 3140 for inspiration by the patient. Projection 3165 is preferably made of the same material as tube 3141 forming flow path 3140, e.g., an acrylic material, and more preferably is molded as a part of tube 3141. Nozzle 3160 is preferably provided with a configuration that facilitates aerosol generation and dispersion appropriate for the tube dimensions.

Tube 3141 preferably provides mouthpiece 3110 with a cylindrical cross section preferably larger than the aerosol plume delivery into the patient's mouth. Tube 3141 need not have a uniform cross section, but desirably has minimal pressure drop there across (excluding any pressure drop across sensor 3300). Alternate embodiments for the cross section of mouth end 3142 may include circular, oval or

flattened oval cross sections or other configurations developed to provide a good seal between the patient's mouth and flow path 3140 so that the patient's inspiratory and expiratory flow passes substantially through tube 3141 along path 3140.

Flow sensor 3300 may be any sensor that provides a measure of flow at a rate of from about 0 to about 800 liters per minute. Flow sensor 3300 is located in flow path 3140 where it will not interfere with the delivery of aerosol to the patient, yet is able to measure both inspiratory and expiratory flow. In the preferred embodiment, sensor 3300 includes a flow resistor device that provides laminar air flow across sensor 3300, comprising three screens, 3304, 3305, and 3306, and two pressure ports 3302 and 3303. Associated with sensor 3300 are a conventional pressure differential transducer 3301 and circuits for obtaining a flow measurement (see FIGS. 4 and 6, transducer 3301 is illustrated in FIG. 2 for reference). Screens 3304, 3305 and 3306 are oriented perpendicular to air flow path 3140, spaced apart 1/4" in parallel and secured to the inside of tube 3141 so that they extend across the cross sectional area of path 3140. Referring to Fig. 1, tube 3141 is assembled by gluing together, in axial alignment, mouth tube section 3110, screen 3306, tube section 3111, screen 3305, tube section 3112, screen 3304, and end tube section 3144 whereby the lengths of tube sections 3111 and 3112 define the spacing between the screens.

Screen 3305 is a resistor screen across which a differential pressure is measured at ports 3302 and 3303 to obtain a measure of the flow rate. Screens 3304 and 3306 provide a laminar air flow across screen 3305 and through sensor 3300 which is suitable for obtaining air flow measurements. Port 3302 is located between screens 3306 and 3305, and port 3303 is located between screens 3305 and 3304. Referring to FIG. 2, ports 3302 and 3303 are respectively connected to transducer 3301 by conventional

flexible tubes 3307 and 3308 having about a 3 mm inner diameter and provide the differential pressures developed across resistive screen 3305 to transducer 3301. The differential pressures, preferably in the range of plus or minus 10 cm of water, are then used to provide a voltage proportional to flow through path 3140, and the sign of the voltage determines the direction of flow. One such preferred differential flow transducer 3301 is model No. NPH-8-2.5DH, commercially available from Novasensor of Fremont, California. The flow through pathway 3140 may be sampled at 60 Hz to obtain the flow rate measurements.

Other forms of such a sensor 3300 may be other forms of a pneumotachograph, e.g., a temperature compensated device, or a thermal wire air flow measurement system. A pneumotachograph is a known sensor having a pneumatic resistor interposed in an air flow, such as a resistor screen, that maintains a laminar air flow having a pressure drop across the structure. The pressure drop is measured and can be directly related to air flow rates across the structure by the pneumatic equivalent of Ohm's law. Thus, once the sensor is calibrated, the air flow rate can be accurately determined based on the measured pressure drop for any air flowing across the structure within the operating range of the sensor.

In an alternate embodiment (not shown), a suitable differential pressure flow sensor could include, for example, a structure, a venturi device or a flow resistive screen not characterized by laminar flow. However, the raw differential pressure measurement obtained across such a venturi device or the flow resistor is then calibrated to account for the non-linearity of the air flow path so that the calibrated flow data correspond to data from a linear flow path.

In the preferred embodiment, flow path 3140, including mouthpiece 3110, protrusion 3165, and sensor 3300 (optionally not including transducer 3301) may be removable from body 3100 so that it may comprise a disposable part. A

conventional detachable connection, not shown, may be provided. Accordingly, means for interconnecting channel 3154 to valve 3150, such as a male-female snap connection, may be incorporated into the design. Use of a disposable airway is desirable so that it can be cleaned or a new mouthpiece provided. Similarly, if a filter is provided (not shown), that filter may be separately removable from the part for replacement.

Referring to FIGS. 1-5, control electronics 3400 for an embodiment of the present invention are shown. Electronics 3400 include a microprocessor 2000, an external memory subsystem 2100, a decoder circuit 2020, a latch device 2030, a reset circuit 2040, a clock oscillator 2010, a data acquisition subsystem 2200, three LED annunciator subsystems 2300, 2400 and 2500, a solenoid actuator subsystem 2600, an audio speaker subsystem 2700, and a character display subsystem 2800. The discrete components of electronics 3400 are conventional parts having input and output pins which are configured as illustrated in FIGS. 4-11 and described herein, which connections are made in accordance with the instructions provided by the device manufacturers, unless otherwise stated.

Use of CMOS technology for electronics 3400 is preferred because of the low power consumption of such devices. This permits the use of a battery powered, portable, hand-held device for patient use having a size that compares favorably to existing metered dose inhaler devices.

Microprocessor 2000 is provided with suitable software programming that controls the operation of the device. The creation of suitable software to achieve the functions described herein, with reference to the flow charts of FIGS. 12 and 13a-13f as described herein, is believed to be within the ability of a person of ordinary skill in the art.

Optionally, electronics 3400 may include a voltage converter and an associated output port for converting the

digital information to a voltage format compatible for communicating with another microprocessor device, for example, an RS232 port or a facsimile machine (not shown).

Referring to FIG. 4, microprocessor 2000 may be any software controlled device suitable for operating the data acquisition and determination functions and for controlling the operation of solenoid valve 3150 to release the selected number of pulses of medication at the desired points in the patient's inspiratory flow in accordance with the preferred embodiment of the invention. One suitable device for microprocessor 2000 is model no. MC68HC11A1, available from Motorola, Inc., Microcontroller Division, Austin, Texas, the use of which is described herein.

Microprocessor 2000 is preferably configured to run in an expanded multiplexed mode through connection of lines MODA and MODB at pins 2 and 3 to logic one, a reference voltage Vcc of +5 volt fed across a 10 KΩ resistor. Latch device 2030 is preferably an 8 bit device that demultiplexes the address and data information transmitted along port c at pins 9-16 of microprocessor 2000 and allows addressing of the address space of memory subsystem 2100. Latch 2030 is preferably model 74HC373, available from National Semiconductor, Santa Clara, California.

Memory subsystem 2100 preferably has a 64K byte address space and includes two 32K byte non-volatile CMOS RAM devices 2110 and 2120, each containing an internal lithium battery. Preferably, RAM devices 2110 and 2120 each contain a non-volatile clock/calendar that is settable and accessible under software control by microprocessor 2000. In the preferred embodiment, only the clock/calendar of device 2110 is used. Non-volatile RAM devices 2110 and 2120 thus provide for maintaining a date and time record of the data acquired and the operation of the device for subsequent review and evaluation by appropriate medical practitioners. This will enable evaluation of the performance of the device for the delivery of medication and the efficacy of the drug therapy program for the patient, even in the event of

general power loss of electronic control circuits 3400. The clock/calendar feature also can be used to perform the alarm clock feature to indicate to the patient that a dose is to be administered, for example, by reviewing a list of scheduled dosing times. Appropriate RAM devices 2110 and 2120 are preferably models DS1244Y, available from Dallas Semiconductor, Dallas, Texas.

The 64K byte address space of memory subsystem 2100 may be continuously addressed in the following manner. Signal AS at pin 4 of microprocessor 2000 causes the low 8 bits of a 16 bit address to be latched from port c at pins 9-16 of microprocessor 2000 into pins 2, 4, 7, 8, 13, 14, 17, and 18 of latch 2030. The latching of these address bits into latch 2030 allows 8 bits of data from port c, the high address bits from port b (pins 35-42 of microprocessor 2000) and the low 8 address bits from the output at pins 2, 5, 6, 9, 12, 15, 16, and 19 of latch 2030 to be available simultaneously.

Decoder device 2020 is used to decode the write enable WE/, output enable OE/, and chip enable CE/ control lines at pins 27, 22, and 20 respectively of each of RAMs 2110 and 2120. A suitable decoder device 2020 is model 74HC139, available from National Semiconductor, Santa Clara, California. Address line A15 from line PB7 at pin 35 of microprocessor 2000, is input to line 1A at pin 2 of decoder 2020 and is used to determine which 32K byte RAM bank to select for each memory access. Valid WRITE/, READ/, CE/1, and CE/2 signals respectively coming from pins 10, 9, 6, and 7 of decoder 2020 are all active low and are valid only when the signal E from pin 5 of microprocessor 2000 is raised active high. This procedure ensures that memory subsystem 2100 will be accessed only during valid memory references.

Clock 2010 provides a clock input for microprocessor 2000. Preferably, clock 2010 is a CMOS oscillator having a frequency of 8.0 MHz. A suitable device for clock 2010 is model MX045, available from CTS Inc., Japan.

Referring to FIGS. 4 and 5, reset circuit 2040 provides a power-on reset function. Reset circuit 2040 includes a reference voltage Vcc, resistor 2041, capacitor 2042 and switch 2043. When the system is turned on, a transient pulse from ground to voltage Vcc is generated. Vcc is preferably +5 volts, resistor 2041 is preferably 1 KΩ, and capacitor 2042 is preferably 2.2 microfarads. Resistor 2041 thus presents a logic high signal to the non-grounding lead of capacitor 2042 when power is applied to the system. However, the potential across capacitor 2042 does not change instantaneously and a ground potential is presented to the RESET/ line at pin 17 of microprocessor 2000 until capacitor 2042 charges. This provides for a reset of microprocessor 2000, its software routines, and the electronic system of the device. A manual reset may be obtained at an arbitrary time by closing switch 2043. This provides for discharging capacitor 2042 to obtain a transient ground pulse for resetting microprocessor 2000.

Referring to FIGS. 4-11, microprocessor 2000 is configured to be connected to and control data acquisition subsystem 2200, LED annunciator modules 2300, 2400, and 2500, solenoid control module 2600, speaker module 2700, and character display subsystem 2800.

With reference to FIGS. 4 and 6, data acquisition subsystem 2200 includes a 12 bit analog to digital converter (ADC) 2210 and an analog circuit 2220. ADC 2210 is preferably a model LTC1290, available from Linear Technology Corporation, Milpitas, California and is interfaced to microprocessor 2000 via a three wire serial interface and a chip select line. The serial interface includes control lines serial clock SCLK, data in DIN, and data out DOUT, respectively at pins 18, 17, and 16 of ADC 2210. These control lines are connected to lines serial clock SCK, master out slave in MOSI, and master in slave out MISO at pins 24, 23, and 22 of microprocessor 2000.

Lines SCK, MOSI and MISO of microprocessor 2000 are internally associated with the serial peripheral interface

(SPI) feature of microprocessor 2000 which is programmed to run as "master" in this embodiment. The SPI allows a stream of bytes of arbitrary length to be simultaneously sent and received by microprocessor 2000. Bytes sent serially to the DIN input of ADC 2210 are interpreted as digitized data points.

Input CS/ at pin 15 of ADC 2210 is connected to line A7 at pin 27 of microprocessor 2000 and is manipulated under software control to facilitate communication to and from ADC 2210. A logic low signal on this line causes data to be simultaneously shifted in and out of lines DIN and DOUT, respectively. A logic high signal on this line cause ADC 2210 to ignore data present on line DIN and causes the DOUT line to float.

Analog module 2220 generates a voltage proportional to flow across sensor 3300 as determined by a differential strain gage pressure transducer 2222. Module 2220 includes an instrumentation amplifier 2221, pressure transducer 2222 (corresponding to element 3301 illustrated in FIG. 4), a constant current source 2223, a low pass filter circuit 2224, and a gain and offset circuit 2225.

Transducer 2222 is preferably a wheatstone bridge strain gage pressure transducer capable of producing a signal over a pressure range of plus or minus 10 inches of water. One such transducer device is model NPH-8-02.5DH available from Novasensor Inc., Fremont, California. Transducer 2222 is excited by constant current source 2223, an operational amplifier 2231 configured to provide approximately 1.5 ma. Input to transducer 2222 are the pressures communicated through tubes 3307 and 3308 from ports 3302 and 3303 of sensor 3300 which are converted to electrical signals by transducer 2222. The output electrical signals produced at pins 4 and 10 of transducer 2222 are provided to input pins 3 and 6 of instrumentation amplifier 2221. Input at pin 5 of transducer 2222 is a reference voltage Vcc of +5 volts fed across a resistor 2230 having a resistance of 1.5 KΩ.

Instrumentation amplifier 2221 is preferably a model LT1101 available from Linear Technology, Fremont, California, and is configured with a reference voltage -Vcc of -5 volt input to pin 4, and a reference voltage Vcc of +5 volts input to pin 5, respectively fed across parallel decoupling capacitors 2233 and 2234 each having a capacitance of 0.1 microfarads. Amplifier 2221 provides a gain of about 100.

The outputs at pins 1 and 8 of amplifier 2221 are fed forward to filter 2224. Filter 2224 is configured as a 28 Hz, 4 pole active low pass filter having a gain of about 4. This circuit acts as an anti-aliasing filter prior to the anticipated 60 Hz sampling rate of analog to digital conversion. Filter circuit 2224 includes two operational amplifiers 2236 and 2237 having identical circuit configurations that are connected in series as illustrated in FIG. 6. Resistors 2240 are 51.1 KΩ, resistors 2241 are 64.9 KΩ. Resistors 2242 are 102 KΩ. Capacitors 2243 are 0.22 microfarads and capacitors 2244 are 0.022 microfarads.

The filtered output signal is passed through circuit 2225 to offset adjust the signal for a final gain of about 1200. Circuit 2225 includes amplifier 2238 configured as illustrated in FIG. 6. Resistor 2250 is 100 KΩ, resistor 2251 is 330 KΩ, capacitor 2252 is 0.01 microfarads, resistor 2254 is 100 KΩ, and potentiometer 2253 has a maximum resistance of 100 KΩ. Potentiometer 2253 is preferably a conventional multiturn potentiometer that provides for nulling the offset prior to beginning any flow measurement. The function could be provided by a digitally controlled potentiometer under software program control. The four operational amplifiers of circuit 2220 are preferably contained within a single device, part No. LP324, available from National Semiconductor, Santa Clara, California.

The differential pressure inputs of transducer 2222 are in communication with airway 3140 through port 3302 and 3303 via tubes 3307 and 3308. Thus, in operation, air flow through sensor 3300 causes a pressure drop across resistor

screen 3305 that varies with the flow. Analog module 2220 thus provides an output signal FLOW having a voltage proportional to flow and a sign, plus or minus, that indicates the direction of flow being detected.

Output FLOW of circuit 2220 is fed to pin 1 of ADC 2210 via channel 1 of the internal analog multiplexor. This input is configured under program control to function in a bipolar, singled ended mode.

Referring to FIGS. 4 and 7-9, LED annunciator modules 2300, 2400, and 2500 are similarly configured and each includes respectively one transistor switch 2301, 2401, and 2501 controlling a single light emitting diode 2302, 2402, and 2502, where each of diodes 2302, 2402 and 2502 emit light at a different color of the visible spectrum, more particularly amber, green and red respectively. Appropriate LEDs are part numbers LN48YCP (amber), LN48GCP (green) and LN48RCP (red), each available from Panasonic, Japan.

For each of modules 2300, 2400 and 2500, each switching transistor is driven, via a base current limiting resistor, by the corresponding digital output at each of pins 20, 31, and 21 of microprocessor 2000. When the transistor conducts, current flows through the LED to ground through a collector current limiting resistor. Each of the circuits are respectively configured with transistors 2301, 2401, and 2501 having base resistors 2303, 2403, and 2503 of 1.5 KΩ, LEDs 2302, 2402, and 2502 in series with collector resistors 2304, 2404, and 2504 each having 240 Ω in series with reference voltage Vcc of +5 volts, and the transistor emitters tied to ground.

Referring to FIGS. 4 and 10, microprocessor 2000 controls the operation of solenoid valve 3150 under software control through module 2600. In operation, module 2600 causes solenoid valve 3150 to deliver a pulse of aerosolized medication when the digital output line PA5 at pin 29 of microprocessor 2000, delivered to module 2600 as line SOLO, is brought high. Module 2600 includes amplifier 2610,

current limiting base resistor 2621 (200 Ω), switching transistor 2620, resistor 2630 (12 KΩ) and capacitor 2631 (3300 picofarads) connected in series, and collectively in parallel with diode 2640 and in parallel with the inputs of solenoid valve 3150 as illustrated in FIG. 10. Solenoid valve 3150 is preferably model No. LFHA1200160H, available from Lee Corporation, Westbrook, Connecticut, and includes an integral solenoid and valve mechanism wherein the valve is operated by the solenoid. Amplifier 2610 is preferably an amplifier from device model LP324 available from National Semiconductor, Santa Clara, California, and is configured in a voltage follower mode. The combination of resistor 2630, capacitor 2631 and diode 2640 suppresses surges during the firing of solenoid valve 3150. Diode 2640 is preferably a conventional model No. 1N4004 diode.

When input signal SOLO is brought high, transistor 2620, preferably a model 2N222 available from Motorola, Inc, Phoenix, Arizona, conducts to cause current to flow through solenoid valve 3150. This causes valve 3150 to open to release a dosage of medication from canister 3200 through flow system 3130 for delivery to and inspiration by the patient. When signal SOLO is brought low, the current stops and valve 3150 closes, terminating the dosage pulse. In accordance with the present invention, the operation of the solenoid valve 3150 is controlled by microprocessor 2000 under software control to provide for improved delivery of aerosolized drugs to the patient's lungs.

Referring to FIGS. 4 and 11, speaker module 2700 is a one transistor amplifier controlling an audio transducer 2740. A preferred transducer 2740 is model No. EAF-14RO6C, available from Panasonic, Japan. Module 2700 includes transistor 2720, preferably a model 2N222 available from Motorola, Inc., Phoenix, Arizona, configured with a base current limiting resistor 2730 having 1.5 KΩ, a reference voltage Vcc of +5 volts fed across, in parallel, collector resistor 2730 having 300 Ω and audio transducer 2740. The transistor emitter is grounded. Input to module 2700 is

signal TONE from line PA4 at pin 30 of microprocessor 2000. When transistor 2720 conducts, current flows through collector resistor 2730 and speaker 2740 through the collector of transistor 2720. The current through speaker 2740 is thus the collector current of transistor 2720 when saturated minus the current through resistor 2730. Line PA4 of microprocessor 2000 will be switched under program control so as to introduce a square wave of varying period to the input signal TONE. In this manner, an audible tone proportional to airway flow will be generated.

The audible tone is useful for cuing the patient to breathe in consistent patterns from time to time. In an alternate embodiment, a learning sequence can be programmed into microprocessor 2000 whereby a preselected signal TONE is generated to teach the patient to breath in accordance with a desired breathing pattern for optimal delivery of the particular drug to be administered. Thus, the flow detected can be compared to the preselected signal TONE such that feedback techniques, e.g., using the LED modules, can be use to train the patient to breath in a desirable manner.

In alternate embodiments, speaker 3740 could be replaced by a piezoelectric sheet or material capable of producing audible vibrations or tactile vibrations, the latter being particularly useful for deaf patients.

Referring to FIG. 4, character display subsystem 2800 allows bytes of numeric character data to be sent via the SPI of microprocessor 2000 to a multisegment LED character display 2830. A preferred display 2830 is a model No. NSM2416, available from National Semiconductor, Santa Clara, California. The byte representing a single character to be displayed is sent to shift register 2810 via the SPI of microprocessor 2000. This serial interface is configured in a unidirectional manner so that data can be provided by microprocessor 2000 but no data can be sent to microprocessor 2000 over line MISO. All data sent over the SPI will appear on input line DIN at pins 1 and 2 of shift register 2810 and will be clocked in. However, data will

only be loaded into display 2830 when the digital output line PD5 at pin 25 is asserted by being brought low. Each byte sent to shift register 2180, preferably model no. 74HC164, available from Motorola, Inc., Phoenix, Arizona, intended for character display must contain the ASCII code of the character to be displayed in bits <0:4> and the two bit position address (00 = display position 0; 11 = display position 3) of the display location in which the character is to appear in bits <5:6>. The most significant bit (bit <7:7>) is ignored. The outputs of shift register 2810 and display 2830 select line are conditioned by buffers 2820, (preferably part No. 74HC244, available from National Semiconductor, Santa Clara, California). This is done to allow CMOS level signals from microprocessor 2000 and shift register 2810 to drive inputs of the TTL display 2830.

In an alternate embodiment, display module 2800 may be configured under appropriate software instruction (not shown) and with additional hardware and wire connections so that the full set of ASCII coded bits can be transmitted for providing visual prompt alphanumeric information to the patient and to display various measured parameters to the patient and the medical examiner. Such a display module 2800 could be used to instruct the patient how to use the device for measuring a pulmonary function, specifically FEV1, or to obtain a desirable inspiratory flow. These instructions could include, for example, "take a breath now" indicating that the device is ready, "hold your breath longer" during an inspiratory pause period or other messages, for example, whether or not to breath harder on expiration. Thus, in addition to displaying the number of does remaining, display module 2500 can be used on the one hand to prompt the patient to breath in accordance with selected flow patterns for measuring specific pulmonary functions, and on the other hand to prompt the patient to breathe consistently from breathe to breath and thus optimize use of the device for the intended drug therapy.

Further, display module 2800 also could be used under appropriate software programming (not shown) to display the amount of medication dispensed or given effectively, which may differ from the amount dispensed, and the amount of medication remaining, and provide a clinical acuity index more detailed than that provide by LED annunciator modules 2300, 2400 and 2500. Also, display module 2800 be used to instruct the patient to contact the medical examiner in the event of a determined lack of improvement in the patient's measured pulmonary functions over a predetermined period of time during the course of treatment, a determined decline in condition or a repeated inability to deliver medication in either or both of ProgBreathMode or CalBreathMode (as described below).

Similarly, display module 2800 can provide the patient alphanumeric information regarding the times and dates medication is to be administered, battery condition, and diagnostics for the condition and operation of the device, and, in conjunction with microprocessor 2000 and speaker 2740, generate a tone when the conditions require servicing the device or a battery needs to be changed.

Referring to FIGS. 12 and 13A-13E, a flowchart and program subroutine calling chain for operation of an embodiment of the present invention are illustrated. Subroutines 100 automatically perform system initialization on Reset. Control then transfers to system main loop IdleLoop 000 which repetitively executes subroutines CheckAlarm 200, GetDataPoint 300, CheckThreshold 400, IntegrateOn 500, LoggingOn 600, ProcessBreath 700, IntegrateOff 1000, and LoggingOff 1010, in accordance with the algorithm described below, forever.

Subroutine 200 checks the system's real time clock and compare the current time (in hours) to a stored list of recommended dosing times for the patient and the selected medication. If the current hour appears on this list, subroutine 210 causes microprocessor 2000 to provide a signal TONE to generate an audible alarm on module 2700 once

for that hour. In the present embodiment the alarm serves as a recommendation to the patient that a dose is to be taken, but does not control or alter the function of the rest of the program. After the alarm clock functions have been performed, control transfers to subroutine GetDataPoint at branch point 300 which measures the instantaneous flow in airway 3140.

Referring to Figs. 12 and 13C, flow is measured by the series of routines beginning with GetDataPoint. These routines perform data acquisition, signal processing, calibration, integration, data logging and information display functions.

Routine GetDataPoint begins by holding for a real time interrupt WaitForRTI, resulting in a 60Hz sample rate because of initial configuration by the ConfigRTI routine executed during the Reset sequence. On a 1/60 second real time event mark, a flow data point is acquired from ADC 2210 by routine AcquireSignal.

The datapoint obtained from ADC 2210 by AcquireSignal is a 12 bit signed quantity (without sign extension). Signal processing begins by removing the lower two bits, which are assumed to be noise, by routine TrimLowBits, and proceeds with subsequent application of an 8 element moving average low pass digital filter by routine LowPassFilter.

The trimmed, low pass filtered flow data point value is then converted to its absolute value by routine AbsoluteValue and the sign bit stored for subsequent use by decision points requiring flow direction information (sign bit unity => inhalation, sign bit zero => exhalation).

The absolute value of the trimmed, filtered flow data point is then converted to a binary representation of flow in liters per minute by application of routine CalFlow. A rough conversion is first obtained by multiplying the uncalibrated value by two. A more accurate calibration is possible by applying correction factors to this rough calibrated value as a function of value. In the limit, one

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(ProgBreathMode), the routine ProcessInspiration attempts to deliver drug at pre-programmed absolute flow and volume firing points. This process begins at branch point 810 where the flow and volume firing points pre-programmed in non-volatile system memory are copied into vectors FlowPoints and VolPoints. This process results in the production of "scheduled flow/volume firing points." An audible tone proportional to the instantaneous measured airway flow is started at point 820. Routines 830 continuously monitor the measured flow rate and volume during the inspiration and deliver drug as each successive pre-programmed flow/volume firing point now in vectors FlowPoints and VolPoints is reached. A flow/volume firing point is defined as a point during inspiration where both the instantaneous flow rate and flow volume are greater than or equal to a preprogrammed flow rate and flow volume pair.

Routines 830 then deliver drug as each firing point is reached. Routines 840 decrement the shot counter which provides a numeric character display for the user indicating the number of doses of drug remaining, and advance pointers stored at NxtFireFlow and NxtFireVol. These pointers will then be indicating the next flow/volume firing point (if preprogrammed) stored in vectors FlowPoints and VolPoints.

Flow/volume firing information for the Programmed Breath Mode is stored in the Firing Point Data. The FireCount variable encodes the maximum number of possible firing points. Vectors FireFlow and FireVolume together encode flow/volume firing point pairs where FireFlow[i] and FireVolume[i] refer to firing point i. Flow rate is expressed in liters per minute, flow volume in liters. Preferably, as each firing point is reached, a uniform pulse is generated. In an alternate embodiment, variable size pulses may be generated in accordance with a selected schedule relating the time of delivery of the successive firing points to the desired location of deposition of the aerosol particles.

If the system is currently in CalBreathMode, i.e., calibration breath mode, control is transferred at branch point 710 to the routines ComputeCalPoints at branch point 800. These latter routines load the FlowPoints and VolPoints flow/volume firing point data arrays. Instead of copying pre-programmed flow/volume firing point data into the FlowPoints and VolPoints arrays as was done by routine ComputeProgPoints, routines at branch point 810, routines ComputeCalPoints at point 800 calculate flow/volume firing points based on the flow/volume maxima achieved during the preceding breath. This process results in the production of "scheduled flow/volume firing points."

Vectors PctFireFlow and PctFireVol contain the pre-programmed percent of maxima information used by routines ComputeCalPoints to make the flow/volume firing point calculations. These percent factors are encoded as the number of right shift operations needed to generate the desired percentage from a binary representation of the original value. Thus, unity represents 50%, two represents 25%, three represents 12.5% and so on.

Routines ComputeCalPoints apply percentage information contained in vectors PctFireFlow and PctMaxFlow to flow and volume maxima, respectively, measured during the last breath. A plurality of absolute flow/volume firing points (the exact number of firing points determined, as in ProgBreathMode, by the preprogrammed variable FireCount) are constructed, and placed in the FlowPoints and VolPoints vectors.

Control is then transferred to routines 820 and 830, and are again used, as they were in ProgBreathMode, to start an audible tone proportional to measured airway flow (routine EnableTone at branch point 820) and to deliver drug at the now appropriate flow/volume firing points (routines 830). The flow/volume firing points now resident in vectors FlowPoints and VolPoints are again consulted by routines 830 and used to trigger solenoid 3150 upon satisfaction of these thresholds.

It is the plurality of flow/volume firing point data loaded into the FlowPoints and VolPoints vectors by routines 800 and 810 respectively that distinguishes the behavior of the system during CalBreathMode and ProgBreathMode. In particular, during ProgBreathMode an attempt is made to deliver drug at invariant, pre-programmed firing points. During CalBreathMode, an attempt is made to deliver drug at flow/volume firing points determined through the application of pre-programmed percentage constants to the flow and volume maxima determined during the previous breath.

After all single inhalation scheduled drug deliveries have been made, or when measured flow changes direction, the audible tone proportional to flow is disabled by routine 850 and the appropriate mode for the next breath is determined at branch point 700. If some drug was delivered, it is assumed that the patient was making an acceptable inspiratory effort (even though all scheduled drug deliveries may not have taken place). In the case that some drug was delivered, the next mode will be ProgBreathMode, selected by routine ProgMode at branch point 720. On the other hand, if no drug was delivered, the assumption is made that the patient made an inadequate inspiratory effort, and was unable to meet any of the flow/volume firing point criteria for the previous breath. In this case, CalBreathMode is selected for the next breath by routine CalMode at branch point 730.

By entering CalBreathMode, the system is accommodating to individual patient characteristics when the patient has demonstrated an inability to generate sufficient inspiratory flow and volume to meet even one scheduled flow/volume firing point. By calculating new firing points as a fraction of flow/volume parameters actually achieved during the previous breath, the chance of achieving a drug delivery during the subsequent breath becomes more likely. In other words, if none of the more desirable (i.e., relatively late in the cycle) scheduled flow/volume firing points can be met by a patient's inspiratory effort, then

new scheduled flow/volume firing points occurring earlier in the inspiratory cycle, i.e., at relatively lower flow rates and flow volumes, are more desirable than no drug delivery at all.

In accordance with the present invention, if no drug is delivered during an inspiration in the CalBreathMode, CalBreathMode will again be entered, and new scheduled flow/volume points corresponding to lower flow rates and volumes will be calculated based on the new flow/volume maxima achieved during the most recent previous breath. This strategy virtually ensures that some drug will be eventually delivered, even if the patient's inspiratory effort is deteriorating from breath to breath.

Referring to Figs. 12, 13B, and 13D, after selection of the next breath mode by routines ProgMode at point 720 or CalMode at point 730, the integration process is stopped by routine IntegrateOff at point 1000 and the data logging stopped by routine LoggingOff at point 1010. During each breath, a log of all measured flow data is kept in an array into which is also stored the time and date, mode and (flow) points in the array where drug was delivered.

This completes the description of the behavior of the software branching routines during an inhalation.

Referring to FIGS. 12, 13B, and 13D, if an exhalation is detected at decision branching point 700, control is transferred to exhalation handling routines ProcExpiration at branching point 900. Routine EnableTone at point 910 activates an audible tone proportional to measured airway flow. Flow is continuously measured and data points are logged until flow direction reverses. Routines 920 detect peak flow by noting the flow prior to the point of flow reversal. This peak flow point is mapped into a three level clinical acuity index by routines DisplayAcuity at point 940 through the use of pre-programmed constants stored at AcuityGreen, AcuityAmber and AcuityRed.

If the measured peak flow is greater than or equal to the value stored at AcuityGreen, a green light emitting

diode is illuminated by routines 940 indicating that the patient's condition is nominal. If the measured peak flow is greater than or equal to the value stored at AcuityAmber, and less than the value stored at AcuityGreen, an amber light emitting diode is illuminated by routines 940 indicating that the patient's condition is marginal. If the measured peak flow is greater than or equal to the value stored at AcuityRed, and less than the value stored at AcuityAmber, a red light emitting diode is illuminated by routines 940 indicating that the patient's condition is unacceptable.

Subsequent to display of the acuity index, the integration is stopped by routine IntegrateOff at point 1000. Note that volume information is not used during the processing of an exhalation by this embodiment. However, in an alternate embodiment, such volume data could be used to calculate valuable pulmonary function indices such as the FEV1 (volume exhaled in one second) and vital capacity (VC). The FEV1 could be used to provide more clinical acuity information to the patient than the three level index based on peak expiratory flow now displayed. Further note that, although the volume information is not being used to calculate the FEV1 in this embodiment, the FEV1 could be calculated later through analysis of the logged flow points of data.

Control then continues to routine LoggingOff at point 1010 which stops data logging, as was done during inhalation mode described earlier.

The preferred embodiment makes extensive use of internally programmed constants which influence the system behavior. These constants are readily changed in the current embodiment through the use of a microprocessor emulator system which allows an MS-DOS computer to be used to arbitrarily modify a plurality of non-volatile system memory locations containing either program or data.

It is intended that the suitable software program be flexible in design so that the system can be configured for

use with a particular patient by selecting certain processing subroutines, calibration coefficients, and operating parameters from an external source. Thus, the main program can use the selected material to accommodate patient specific or drug specific requirements in different applications to treat predetermined medical conditions. Thus, the software controlling the device preferably can be configured or customized for a specific use by a specific patient. Accordingly, when the device is used for a different patient or medication or both, the software can be reconfigured for such use.

In another alternate embodiment of the present invention, the software is programmed to measure pulmonary function periodically, preferably prior to each administration of a dosage, and look for changes in the detected flow patterns and measured pulmonary functions of the patient during the course of treatment. Those detected changes are then used to modify the treatment parameters in accordance with the improved or degenerated condition of the patient. For example, the dosage per administration and the frequency of administration could be adjusted as indicated by detected changes in the patient's condition. Similarly the dosage could be adjusted from administration to administration by measuring the time between administration to determine a maximum allowed dosage based on accepted medical practices.

In an alternate embodiment, the software routine could be prepared to operate in the calibrated breath mode all the time. In this embodiment, a first breath flow must be acquired and evaluated to identify initial desired threshold firing point or points in the measured flow to administer the medication for the most efficacious inspiration. That information is used during a second inspiratory flow to actuate solenoid valve 3150 to administer the medication when the flow in a second acquired inspiration corresponds to the identified threshold desired points. In this embodiment, speaker module 2700 could be

driven by microprocessor 2000 to prompt the patient to conduct the second inspiration with the same breathing pattern used in the first measured inspiration by recording the flow rate tones of the first inspiration and regenerating those tones in the second breath.

Measuring flow without drug delivery also provides several advantages. For example, displaying the visual acuity index corresponding to the measured expiratory flow can instruct the patient to seek immediate medical attention. Thus, the patient is advised of the need for medical attention when they might not otherwise realize that they need it. This is of particular concern when a patient has just been to a doctor and would not think it necessary to return to the doctor so soon, waiting instead for the prescribed medication to take effect. For another example, it permits obtaining an initial or baseline breath pattern for the patient based on one or more inspirations and expirations e.g., FEV1, vital capacity, and peak expiratory flow. If more than one breath pattern is used to obtain the baseline, the recorded data can be averaged to form the baseline pattern. This baseline can be used to determine gross changes in the patient's pulmonary functions which can be displayed to the patient or relayed to the medical examiner or both to provide an ongoing assessment of the therapy program.

Obtaining a baseline pattern provides several advantages. First, the determined pattern can be used to determine the optimum point or points in the inspiratory flow for delivery of aerosolized medication for the selected medication in its particular application. Thus, the administration of the drug can be based on the patient's actual flow patterns, including inspiratory flow, inspiratory pause, and expiratory flow, and automatically released when the predetermined point or points in the flow occurs. This permits adapting the device to the patient and providing a more effective means for delivering aerosolized medication.

Second, the patient's determined baseline flow pattern can be used as a predictor to account for changes in the patient's breath patterns. Thus, a subsequent inspiration, during which the aerosolized medication will be delivered, can be detected in real time and compared to the previously determined baseline pattern. Any differences in the patterns can be identified. The baseline pattern can then be used to predict the remaining portion of the real time inspiratory flow taking into account the prior deviations in the real time inspiration. This permits adjusting in real time the actual point or points to administer medication, as compared to basing the administration on the occurrence of the predetermined optimal point or points derived from the baseline pattern. Thus, breath to breath variations in the patient's breathing patterns can be identified and used to adjust the administration of medication.

Third, the determined pattern can be used to generate an audible prompt, for example, a tone generated by speaker 2740 that changes in volume or frequency to correspond to changes in the predetermined baseline breath pattern. Thus, the tone can be used to prompt the patient to follow the previously determined baseline breathing pattern so that the delivery of aerosolized medication can be predictably delivered at the desired point or points in the patient's breathing pattern. The prompt, based on the predetermined breathing pattern, thus helps improve the efficiency of the drug delivery.

Fourth, the determined baseline pattern can be compared to a preferred ideal breathing pattern for optimal delivery of the medication. If substantial differences are found to exist, which differences might affect the efficacy of the drug, the prompt then could be used to drive the patient's breathing pattern, i.e., to prompt the patient to modify his or her regular "baseline" breathing pattern to conform more or less to the ideal desired pattern for that

medication. Thus, the prompt can improve the efficiency of the drug delivery.

In addition, by recording a series of actual inspiratory and expiratory flow data taken over extended time periods, with or without the contemporaneous administration of medication, trend data can be obtained for analyzing the relative success of the drug therapy. This can then be used by microprocessor 2000 in accordance with its software instructions to alter the drug therapy, for example, the dosage of the medication delivered with each administration or the frequency of administration or both. Also, the trend data can be used by the medical examiner to provide additional data regarding the drug therapy to study the drug therapy originally prescribed and to alter the drug therapy as necessary.

Microprocessor 2000 also may be programmed to review the history of the last several administrations of medication prior to an indicated administration to prevent a patient from administering an overdose of medication or to indicate to the patient that insufficient amounts of medication have been administered.

In an alternate embodiment, each canister 3200 may be provided with a battery supply (not shown) and appropriate electrodes to interface with a corresponding receptacle with electrodes on base 3100 (not shown) for powering some portion or all of electronics 3400 of the device. In one embodiment, the battery supply has an expected lifetime that will be sufficient to actuate whatever electromechanical valve is used to administer all of the contents of the canister, and, where appropriate, perform the anticipated flow measurements taken with or without administration of medication, for a given course of therapy involving that particular medication. This advantageously provides for an adequate power supply for operation of the device with a particular medication without requiring the patient to obtain a supply of batteries for use and without regard to what medication is to be

administered. In another embodiment, the canister battery is used for example, to power the electromechanical device used to actuate the valve to release aerosol medication, but not to power the flow measuring electronics, the latter being powered by a separate battery located in base 3100 (not shown).

It has been discovered, using the method of cascade impingement to determine an aerodynamic diameter, that by delivering the aerosolized medication in a series of pulses, as contrasted with a single metered dose, the respirable fraction of the delivered aerosolized compound is substantially increased. More particularly, it has been discovered that the aerosol particle size distribution in a pulse sequence is related to the duration of the pulse within the sequence and can be changed by adjusting the duty cycle of the pulses used to generate the aerosol. This effect may be due to more rapid evaporation of propellent or carrier during a short duty cycle pulse sequence as compared with a single pulse.

In one example, a conventional metered dose inhaler device was compared to a device of the present invention using the method of cascade impingement. It was empirically determined that the metered dose inhaler produced a respirable fraction of about 36%. In contrast, the device in accordance with the present invention, operating to deliver the same dose (by weight) in a pulsatile fashion having four uniform discrete pulses, each pulse having a duty cycle of 13% having a pulse width of 112 msec, corresponding to an on time of 14.56 msec and an off time of 97.44 msec, provided a respirable fraction of about 41%. This is believed to be a substantial improvement in aerosol drug delivery.

The method of cascade impingement can be used in an iterative manner to determine empirically the pulse parameters for maximizing the respirable fraction of the aerosolized compound to be delivered. It should be understood, however, that the term "maximized respirable

fraction" refers to a selected respirable fraction that is substantially improved as compared to the respirable fraction produced by a standard metered dose inhaler device, but is not intended to refer to an absolute maximum respirable fraction relative to that produced by a metered dose inhaler device.

In accordance with the present invention, valve 3150 is controlled by microprocessor 2000 and is used as a high frequency switch to release a series of pulses of the aerosol medication having a selectable width, shape, and frequency. The pulses are delivered to the patient through nozzle 3160 mouth end 3142 mouthpiece 3110. By selecting the time period and frequency that valve 3150 is open, the pulse width and interval between adjacent pulses can be selected. Having selected for the desired particle size, the patient's breathing pattern can then be used to identify the optimal points or points at which to deliver the pulses of aerosol medication for delivery to the desired locus or loci in the airway. Further, the selected particle size can then be used with an optimal inspiratory flow, inspiratory pause, expiratory flow, and tidal volume to deliver the aerosol medication to the most therapeutically efficacious locations in the patient's airway. It should be understood that each such dose given as a sequence of pulses can be deposited at different loci by changing the delivery schedule with respect to at which point or points in the inspiratory flow the aerosol is delivered for inspration.

Valve 3150 also can be used to control the total dosage delivered during a single administration by providing a selected number of pulses of equal width, or a first selected number of pulses of a first width and a second selected number of pulses of a second width, whether those first and second pulses are delivered in succession, alternately, or randomly, synchronously or asynchronously. Further, valve 3150 could be used to administer the desired dosage over more than one inspiration in the event that the drug therapy requires a dosage that could not be practicably

administered in a single inspiration. Changes in the location or the total dosage can be made through changing the control information provided to solenoid valve 3150 by microprocessor 2000 to produce the desired number and size of pulses in response to the desired delivery schedule.

In accordance with this alternate embodiment of the invention, another function of microprocessor 2000 is to select an optimum particle size and delivery schedule for the medication to be administered for the patient. This is achieved by evaluating the specific medication to be delivered and the nature of the condition, e.g., whether the drug is to be delivered to the large airways, small airways, or both. This function may be enhanced by also evaluating measured flow and determining optimum points in the measured flow to administer the medication, and using that information in a successive inspiratory flow to administer the medication at an appropriate time as discussed herein.

In accordance with an alternate embodiment, the canisters containing the medication could be constructed with an electromechanical valve actuator integral to the canister. Preferably, the actuators are powered by a battery supplied with the canister. In such an embodiment (not shown) the microprocessor would interface with the canister to provide control signals to actuate the valve actuator to select the desired pulse width, interval, and frequency as appropriate for the given circumstances.

In accordance with another embodiment, the apparatus may be provided with a motion detector for determining when the canister of aerosol generating material has been adequately agitated. In this embodiment, the motion detector can be used to prevent delivery of any aerosol until the device indicates that the material has been agitated to cause the material to be sufficiently mixed to provide the desired aerosol. This device is believed to overcome the problem of segregation or sedimentation of the medication and any aerosol precursor, propellant, or carrier material, which is common to canisters containing medication

to be delivered in an aerosol, including metered dose devices. Examples of suitable motion detectors include mercury switches that generate a signal in response to the degree of agitation, which signal is then processed to determine when a sufficient amount of agitation has occurred, whereupon the device is then enabled for delivery of an amount of aerosol.

It also should be understood that other valve switch means for releasing pulses of aerosol could be used in place of an integral solenoid and valve. For example, a solenoid could be used to depress the valve stem of a simple canister valve or to move the canister relative to the valve stem, thereby to provide the appropriate pulses.

One preferred application for the present invention is for bronchodilator therapy for asthma. In this embodiment, the device can be used to select for the proper particle size and dosage by providing a plurality of pulses having different or nonuniform widths at different points in the inspiratory cycle to provide small particles for deposition in the small airways and large particles for deposition in the large airways in sufficient amounts to treat effectively the condition. Measured improvements in pulmonary function can then be used to reduce the dosage both in terms of number of pulses and frequency of administrations.

In another application, the device could be used for treatment of a bronchial constriction in the small airways by providing high frequency pulses during optimal points in the inspiratory flow to produce small particles that deposit in the small airways. Measured improvements in pulmonary function can then be used to reduce the dosage both in terms of number of pulses in a given administration and in the frequency of administrations.

Other anticipated uses of the present invention could be to provide optimal delivery of drugs in aerosol form, based on measured inspiratory and expiratory flow, such as beta-agonists, e.g., albuterol for bronchial-

constriction, inhaled steroids for bronchial inflammation, pentamidine for pneumocystis prophylaxis in patients who have tested positive for HIV, narcotics, e.g., morphine or other opiate derivatives, for patients having chronic pain, allowing for effective self-medication exploiting the rapid onset of an aerosol medication administration technique, and without substantial risk of overdosing, and with providing the medical examiner a record of the drug administration for evaluation in the event of continued therapy. See also, e.g., the medications identified in D. Kohler, Lung (1990), Supp., p. 679. The terms inspiration and inhalation are used interchangeably herein and the terms expiration and exhalation are used interchangeably herein. It also should be understood that in place of a software driven microprocessor the present invention could be implemented using a finite state machine, including without limitation solid state finite state machines.

It also should be understood that the terms aerosol and aerosol generating material are used, in the context of this invention, generally to include the medicinal compound and any carrier or propellent, whether a liquid, gas, or solid material.

One skilled in the art will appreciate that the present invention can be practiced by other than the described embodiments, which are presented for purposes of illustration and not of limitation.

CLAIMS

1. An apparatus for releasing an aerosol from a reservoir of aerosol generating material for inspiration by a person characterized by:

a valve associated with the reservoir for releasing an amount of aerosol generating material from the reservoir to form an aerosol;

a sensor for monitoring inspiratory flow through a flow path;

means for calculating a delivery threshold based on a sensed flow parameter of a detected inspiratory flow;

means for determining whether each detected inspiratory flow is one of a first flow detected following a reset flow event or a subsequent flow detected following a first flow that is not followed by a flow reset event a flow reset event being any of a release of an amount of aerosol, the end of a preselected time interval during which no aerosol was released, and initialization of operation of the apparatus;

means for providing a delivery threshold corresponding to a point in the detected inspiratory flow at which an amount of aerosol is to be released, the provided delivery threshold being a preselected delivery threshold in response to the detected inspiratory flow being a first flow and a calculated delivery threshold in response to the detected inspiratory flow being a subsequent flow, the calculated delivery threshold being calculated based on the preceding detected inspiratory flow; and

means for operating the valve to deliver an amount of aerosol in response to the detected inspiratory flow satisfying the provided delivery threshold.

2. The apparatus of claim 1 characterized in that the calculating means is further characterized by:

means for obtaining the sensed flow parameter of the last detected inspiratory flow in response to the last

detected inspiratory flow not satisfying the provided delivery threshold; and

means for adjusting the provided delivery threshold in response to the obtained flow parameter, thereby providing the calculated delivery threshold for the following detected inspiratory flow.

3. The apparatus of claim 1 characterized in that the delivery threshold further comprises a delivery schedule including the delivery threshold and one or more other delivery points in the detected inspiratory flow following the delivery threshold, and the adjusting means adjusts every delivery point in the delivery schedule and the second determining means determines whether or not the detected inspiratory flow satisfies each delivery point in the delivery schedule so that an amount of aerosol is delivered for each delivery point that is satisfied by the detected inspiratory flow.

4. The apparatus of claim 1 characterized in that the reservoir and the valve means are characterized by a canister having a valve and valve stem and the valve controlling means is characterized by an actuator for moving the valve stem relative to the canister to open and close the canister valve to release an amount of aerosol.

5. The apparatus of claim 1 further characterized by an aerosol flow path having a nozzle for releasing the contents of the reservoir into the inspiratory flow path, characterized in that the valve is interposed in the aerosol flow path for opening and closing the aerosol flow path; and the valve controlling means is a solenoid.

6. The apparatus of claim 1 characterized in that the determining means determines the delivery threshold as one of a selected flow rate, a selected flow volume, and a selected flow rate and flow volume pair, the selected flow rate being less than or at the sensed peak inspiratory flow rate of the first detected inspiratory flow, the selected flow volume being less than or at the peak flow volume of the first detected inspiratory flow.

7. The apparatus of claim 6 characterized in that the delivery threshold is determined to correspond to a selected location of deposition of the aerosol in the person.

8. The apparatus of claim 1 characterized in that the determined delivery schedule includes the delivery threshold and at least one other delivery point in the first detected inspiratory flow and the valve operating means is operated in response to the sensed second detected inspiratory flow satisfying the delivery threshold and each other delivery point.

9. The apparatus of claim 3 characterized in that the valve and the valve operating means are characterized by:

an electromechanical actuator that can be changed at a rate up to 100 cycles per second between a first state for releasing an amount of aerosol generating material and a second state for not releasing an amount of aerosol generating material, the electromechanical actuator being in the first state from a time in the range of from about 10 to about 1000 msecs, thereby to deliver pulses of aerosol having a maximized respirable fraction; and

means for operating the electromechanical actuator to change between the first and second states one or more times in response to the second detected inspiratory flow satisfying each delivery point in the delivery schedule.

10. The apparatus of claim 5 further characterized by a visual display of a measure of the amount of aerosol in the reservoir.

11. The apparatus of claim 5 characterized in that the sensor is a structure interposed in the inspiratory flow path, a means for measuring the differential pressure across the structure, and means for converting the measured differential pressure into an inspiratory flow rate.

12. The apparatus of claim 11 characterized in that the measuring means has a differential pressure sensitivity in the range of about $\pm$25.4 cm of water corresponding to a maximum flow rate up to about 800 liters per minute.

13. The apparatus of claim 12 characterized in that the structure is selected from among one of a venturi section having a first and second cross sectional areas and means for measuring a differential pressure across the first and second areas, a resistive flow screen and characterized in that the means for converting converts the measured differential pressure into a flow rate using an array of predetermined calibration constants.

14. The apparatus of claim 11 further characterized by means for providing a laminar air flow across the structure.

15. The apparatus of claim 14 characterized in that the structure and laminar air flow means are at least three flow resistive screens interposed in series across the inspiratory flow path and the differential pressure is measured across the middle screen.

16. The apparatus of claim 5 characterized in that the sensor is a hot wire anemometer disposed in the inspiratory flow path and means for converting the measured temperature changes into an inspiratory flow rate.

17. A method for delivering an aerosol to a person for inspiration using a device having a supply of aerosol generating material and a valve for releasing an amount of aerosol generating material to form an aerosol and a sensor for detecting the inspiratory flow of a person, characterized by:

monitoring the inspiratory flow of the person;

determining whether each detected inspiratory flow is one of a first flow detected following a reset flow event or a subsequent flow detected following a detected first flow that is not followed by a flow reset event, the flow reset event being any of a release of an amount of aerosol, the end of a preselected time interval during which no aerosol was released, and initialization of operation of the apparatus;

selecting a delivery threshold corresponding to a point in the detected inspiratory flow at which an amount of aerosol is to be released characterized by selecting a

preselected delivery threshold in response to the detected inspiratory flow being a determined first flow and selecting a calculated delivery threshold that is calculated based on a sensed flow parameter of the preceding detected inspiratory flow in response to the detected inspiratory flow being a determined subsequent flow; and

determining whether or not the detected inspiratory flow satisfies the selected delivery threshold and

(i) in response to the detected inspiratory flow satisfying the selected delivery threshold, operating the valve to release an amount of aerosol generating material to form an aerosol; and

(ii) in response to determining that the detected inspiratory flow did not satisfy the selected delivery threshold, calculating a new delivery threshold based on the detected inspiratory flow so that the selected delivery threshold for the next detected inspiratory flow determined to be a subsequent flow is the last calculated delivery threshold.

18. The method of claim 17 characterized in that calculating the delivery threshold is characterized by:

measuring a selected flow parameter of the detected inspiratory flow in response to determining that the detected inspiratory flow did not satisfy the selected delivery threshold; and

adjusting the selected delivery threshold in response to the obtained flow parameter, thereby providing the calculated delivery threshold.

19. The method of claim 18 characterized in that selecting the delivery threshold is further characterized by selecting a delivery schedule including the delivery threshold and one or more other delivery points in an inspiratory flow, and adjusting the provided threshold is further characterized by adjusting each point in the delivery schedule, and operating the valve is further

characterized by operating the valve for each delivery point in the delivery schedule that is satisfied by the detected inspiratory flow.

20. The method of claim 17 characterized in that the supply and the valve are characterized by a canister having a valve and valve stem and operating the valve is characterized by moving the valve stem relative to the canister to open and close the canister valve to release a pulse of aerosol.

21. The method of claim 17 characterized by interposing the valve in an aerosol flow path connecting the contents of the reservoir with a nozzle for releasing the aerosol in the inspiratory flow.

22. The method of claim 18 further characterized by measuring the selected flow parameter to be one of a selected flow rate, a selected flow volume, and a selected flow rate and flow volume pair, the selected flow rate being less than or at the sensed peak inspiratory flow rate of the preceding detected inspiratory flow, the selected flow volume being less than or at the flow volume of the preceding detected inspiratory flow.

23. The method of claim 19 further characterized by:

operating the valve to change between a first state for releasing an amount of aerosol and a second state for not releasing an amount of aerosol one or more times in response to the detected inspiratory flow satisfying each delivery point in the provided delivery schedule, the valve cycling at a rate up to 100 cycles per second; and

controlling the period of time the valve is in the first state to be a time in the range of from about 10 to about 1000 msecs, thereby to release pulses of aerosol having a maximized respirable fraction.

24. The method of claim 17 further characterized by displaying a measure of the amount of aerosol in the supply.

25. The method of claim 17 characterized in that monitoring inspiratory flow is characterized by measuring a differential pressure across a structure in the inspiratory

flow path and converting the measured differential pressure into an inspiratory flow rate.

26. The method of claim 25 characterized in that the structure is selected from among a venturi section having a first and second cross section areas and a resistive flow screen, and converting the measured differential pressure is characterized by converting the measured differential pressures into a flow rate using an array of predetermined calibration constants.

27. The method of claim 25 further characterized by providing a laminar air flow across the structure.

28. The method of claim 27 characterized in that the structure and laminar air flow are at least three flow resistive screens interposed in series across the inspiratory path and measuring the differential pressure across the middle screen.

29. The method of claim 21 characterized in that monitoring inspiratory flow is characterized by determining the temperature change of a hot wire anemometer in response to flow and converting the measured temperature change into an inspiratory flow rate.

30. The method of claim 22 characterized in that determining a delivery threshold is characterized by selecting a delivery threshold that corresponds to a point that will deposit the aerosol at a selected location in the person.

31. An apparatus for releasing an aerosol from a reservoir of aerosol generating material for inspiration by a person characterized by:

a valve for releasing an amount of aerosol generating material from the reservoir to form an aerosol;

a sensor for monitoring the person's inspiratory flow through an inspiratory flow path;

means for determining a delivery schedule, including at least a delivery threshold, for releasing an amount of aerosol in response to a first detected inspiratory flow; and

means for controlling the valve in response to a second detected inspiratory flow satisfying the determined delivery threshold, thereby to release the amount of aerosol during the second inspiratory flow, the second detected inspiratory flow following the first detected inspiratory flow.

32. The apparatus of claim 31 characterized in that the reservoir and the valve means are characterized by a canister having a valve and a valve stem and the valve controlling means is characterized by an actuator for moving the valve stem relative to the canister to open and close the canister valve to release an amount of aerosol.

33. The apparatus of claim 31 further characterized by an aerosol flow path having a nozzle for releasing the contents of the reservoir into the inspiratory flow path, characterized in that the valve is interposed in the aerosol flow path for opening and closing the aerosol flow path; and the valve controlling means is a solenoid.

34. The apparatus of claim 31 characterized in that determining means determines the delivery threshold as one of a selected flow rate, a selected flow volume, and a selected flow rate and flow volume pair, the selected flow rate being less than or at the sensed peak inspiratory flow rate of the first detected inspiratory flow, the selected flow volume being less than or at the peak flow volume of the first detected inspiratory flow.

35. The apparatus of claim 34 characterized in that the delivery threshold is determined to correspond to a selected location of deposition of the aerosol in the person.

36. The apparatus of claim 34 characterized in that the determined delivery schedule includes the delivery threshold and at least one other delivery point in the first detected inspiratory flow and the valve operating means is operated in response to the sensed second detected inspiratory flow satisfying the delivery threshold and each other delivery point.

37. The apparatus of claim 36 characterized in that the valve and the valve operating means are characterized by:

an electromechanical actuator that can be changed at a rate up to 100 cycles per second between a first state for releasing an amount of aerosol generating material and a second state for not releasing an amount of aerosol generating material, the electromechanical actuator being in the first state from a time in the range of from about 10 to about 1000 msecs, thereby to deliver pulses of aerosol having a maximized respirable fraction; and

means for operating the electromechanical actuator to change between the first and second states one or more times in response to the second detected inspiratory flow satisfying each delivery point in the delivery schedule.

38. The apparatus of claim 31 further characterized by a visual display of a measure of the amount of aerosol in the reservoir.

39. The apparatus of claim 31 characterized in that the sensor is a structure interposed in the inspiratory flow path, a means for measuring a differential pressure generated across the structure, and means for converting the measured differential pressure into an inspiratory flow rate.

40. The apparatus of claim 39 characterized in that the measuring means has a differential pressure sensitivity in the range of about $\pm$25.4 cm of water corresponding to a maximum flow rate up to about 800 liters per minute.

41. The apparatus of claim 40 characterized in that the structure is selected from among one of a venturi section having a first and second cross sectional areas and means for measuring a differential pressure across the first and second areas, a resistive flow screen, and the apparatus is characterized in that the means for converting converts the measured differential pressure into a flow rate using an array of predetermined calibration constants.

42. The apparatus of claim 40 further characterized by means for providing a laminar air flow across the structure.

43. The apparatus of claim 40 characterized in that the structure is at least three flow resistive screens interposed in series across the inspiratory flow path and the differential pressure is measured across the middle screen.

44. The apparatus of claim 31 characterized in that the sensor is a hot wire anemometer disposed in the inspiratory flow path and means for converting the measured temperature changes into an inspiratory flow rate.

45. A method for administering an amount of aerosolized medication for inspiration by a person using an inhaler device having a supply of aerosol generating material, a valve for releasing an amount of aerosol generating material to form an aerosol, and means for detecting an inspiratory flow of a person, characterized by:

(a) monitoring the inspiratory flow of the person;

(b) determining a delivery schedule including at least a delivery threshold for the release of an amount of aerosol based on a first detected inspiratory flow;

(c) operating the valve in response to a second detected inspiratory flow satisfying the determined delivery threshold to release an amount of aerosol for inspiration during the second detected inspiratory flow, the second detected inspiratory flow following the first detected inspiratory flow.

46. The method of claim 45 characterized in that the supply and the valve are characterized by a canister having a valve and valve stem and operating the valve is characterized by moving the valve stem relative to the canister to open and close the canister valve to release a pulse of aerosol.

47. The method of claim 45 characterized by interposing the valve in an aerosol flow path connecting the contents of the reservoir with a nozzle for releasing the aerosol in the inspiratory flow.

48. The method of claim 45 further characterized by determining the delivery threshold to be one of a selected

flow rate, a selected flow volume, and a selected flow rate and flow volume pair, the selected flow rate being less than or at the sensed peak inspiratory flow rate of the first detected inspiratory flow, the selected flow volume being less than or at the peak flow volume of the first detected inspiratory flow.

49. The method of claim 48 characterized in that the delivery schedule is characterized by the delivery threshold and at least one other delivery point in the first detected inspiratory flow and operating the valve in response to the sensed second detected inspiratory flow satisfying the delivery threshold and each other delivery point.

50. The method of claim 48 further characterized by:

operating the electromechanical valve actuator to change between a first state for releasing an amount of aerosol and a second state for not releasing an amount of aerosol one or more times in response to the second detected inspiratory flow satisfying each delivery point in the delivery schedule; and

controlling the period of time the valve is in the first state to be a time in the range of from about 10 to about 1000 msecs, thereby to release pulses of aerosol having a maximized respirable fraction.

51. The method of claim 45 further characterized by displaying a measure of the amount of aerosol in the supply.

52. The method of claim 47 characterized in that monitoring inspiratory flow is characterized by measuring a differential pressure across a structure in the inspiratory flow path and converting the measured differential pressure into an inspiratory flow rate.

53. The method of claim 52 characterized in that the structure is selected from among a venturi section having a first and second cross section areas and a resistive flow screen, and converting the measured differential pressure is characterized by converting the measured differential pressure into a flow rate using an array of predetermined calibration constants.

54. The method of claim 53 further characterized by providing a laminar air flow across the structure.

55. The method of claim 54 characterized in that the structure and laminar air flow are at least three flow resistive screens interposed in series across the inspiratory path and measuring the differential pressure across the middle screen.

56. The method of claim 47 characterized in that monitoring inspiratory flow is characterized by determining the temperature change of a hot wire anemometer in response to flow and converting the measured temperature changes into an inspiratory flow rate.

57. The method of claim 48 characterized in that determining a delivery threshold is characterized by selecting a delivery threshold that corresponds to a point that will deposit the aerosol in a selected location in the patient.

58. Apparatus for controlling the respirable fraction of an aerosol characterized by:

a source of aerosol generating material;

a valve, associated with the source, having a first state for releasing an amount of aerosol generating material and a second state for not releasing an amount of aerosol generating material;

means for selecting the relative time the valve is in the first state and the second state to maximize the respirable fraction of a released amount of aerosol, the valve being in the first state for a time selected from between about 10 to about 1000 msec; and

means for cycling the valve between states at a rate at or below 100 cycles per second in response to the selected relative time, to deliver an amount of aerosol having the maximized respirable fraction.

59. The apparatus of claim 58 further characterized by means for providing a trigger signal for operating the cycling means to release an amount of aerosol.

60. The apparatus of claim 59 characterized in that the valve cycling means cycles the valve between states to release more than one amount of aerosol in response to each trigger signal, and characterized in that the relative time selecting means selects a relative time for each amount to be released to provide each amount with a maximized respirable fraction.

61. The apparatus of claim 60 characterized in that the relative time selecting means selects the same relative time for each amount to be released.

62. The apparatus of claim 61 characterized in that the same relative time has a duty cycle selected from among the range of from 8 to 15%.

63. The apparatus of claim 60 characterized in that the valve cycling means and the valve operating means is characterized by an electromechanical actuator.

64. The apparatus of claim 63 further characterized by first structure for containing the reservoir of aerosol and a power supply for operating the electromechanical actuator.

65. The apparatus of claim 59 characterized in that means for providing a trigger signal is characterized by means for selecting a trigger signal corresponding to one or more points in the inspiratory flow forming a delivery schedule so that the aerosol is deposited in a selected location in the patient.

66. A method for controlling the respirable fraction of an aerosolized medication released by an aerosol drug delivery device having a source of aerosol generating material and a valve having a first state for releasing an amount of aerosol generating material to form an aerosol and a second state for not releasing an amount of aerosol generating material, characterized by:

selecting the relative time the valve is in the first state and the second state to maximize the respirable fraction of the amount of aerosol to be released, characterized in that the valve is selected to be in the

first state for a time selected from between 10 to 1000 msecs; and

cycling the valve between states at a rate at or below 100 cycles per second in response to the selected relative time, to deliver an amount of aerosol having the maximized respirable fraction.

67. The method of claim 66 further characterized by cycling the valve to deliver an amount of aerosol in response to a triggering signal.

68. The method of claim 67 further characterized by selecting relative times for more than one amount of aerosol so that each amount has a relative time and a corresponding selected particle size distribution characterized in that cycling the valve is characterized by cycling the valve to release more than one amount of aerosol in response to the selected relative times so that each amount of aerosol is released has the corresponding respirable fraction.

69. The method of claim 68 further characterized by selecting the same relative time for each amount of aerosol.

70. The method of claim 69 further characterized by selecting the same relative time as a duty cycle selected from among the range of 8 to 15%.

71. The method of claim 66 further characterized by providing a triggering signal and cycling the valve to deliver a predetermined number of amounts of aerosol in response to each triggering signal.

72. The method of claim 68 further characterized by providing a triggering signal and cycling the valve to deliver a predetermined number of amounts of aerosol in response to the triggering signal.

73. The method of claim 67 characterized in that providing a trigger signal further comprises selecting a trigger signal corresponding to one or more points in the inspiratory flow forming a delivery schedule so that the aerosol is deposited in a selected location in the patient.

74. A system for dispensing aerosolized medication for inspiration by a patient from a reservoir of medication under pressure characterized by;

a valve in communication with the reservoir for releasing an amount of medication to form an aerosol;

a sensor for monitoring the patient's inspiratory flow; and

means for actuating the valve more than one time to release more than one pulse of aerosol medication in response to the sensed inspiratory flow satisfying a selected delivery threshold.

75. The system of claim 74 characterized in that the valve actuating means is an electromechanical actuator and the reservoir includes a source of energy for operating the electromechanical actuator.

76. The system of claim 75 characterized in that the electromechanical actuator is a solenoid and the source of energy is a battery.

77. The system of claim 74 further characterized by a means for processing signals and controlling the actuating means characterized in that the sensor is a differential pressure transducer and a circuit for providing a measure of the instantaneous flow based on the differential pressure signal corresponding to the sensed flow.

78. A method for dispensing aerosolized medication for inspiration by a patient from a reservoir of medication under pressure having a valve in communication with the reservoir for releasing an amount of medication to form an aerosol, characterized by:

monitoring the patient's inspiratory flow;

comparing the sensed inspiratory flow to a preselected delivery threshold;

actuating the valve more than one time in response to the sensed inspiratory flow satisfying the delivery threshold to release more than one pulse of aerosol medication during the sensed inspiratory flow.

79. The method of claim 78 characterized in that the valve is actuated by an electromechanical actuator and the canister includes a source of energy for operating the electromechanical actuator.

80. The method of claim 78 characterized in that monitoring the patient's flow further comprises measuring a differential pressure of the inspiratory flow across a structure in the inspiratory flow and converting the measured differential pressure signal into a measure of the instantaneous flow.

81. A hand held device for delivering aerosolized medications for inspiration characterized by:

a tube forming a flow path having a mouth end and an open end;

a nozzle disposed in the tube directed toward the mouth end;

a flow transducer disposed in the inspiratory flow path;

a receptacle for receiving a supply of aerosol generating material;

an aerosol flow path extending from the receptacle to the nozzle;

a valve interposed in the aerosol flow path for opening and closing the flow path; and

means for actuating the valve to open and close the flow path for delivering an amount of aerosol out the nozzle.

82. The apparatus of claim 81 characterized in that the valve actuating means opens and closes the valve a predetermined number of times to deliver the amount of aerosol as a predetermined number of pulses in response to each actuation.

83. The apparatus of claim 81 further characterized by means for operating the valve actuating means in response to a detected inspiratory flow.

84. The apparatus of claim 81 characterized in that the valve and valve actuating means are characterized by an

electromechanical device having an open condition for a time selected from the range of from 10 to 1000 msecs and a closed condition.

85. The apparatus of claim 83 characterized in that the flow transducer and the means for operating are characterized by a differential pressure transducer disposed in the inspiratory flow path, means for measuring a differential pressure of a flow across the transducer, and means for converting the measured differential pressure into an inspiratory flow rate.

86. The apparatus of claim 85 characterized in that the differential pressure transducer has a pressure sensitivity in the range of about ±25.4 cm of water corresponding to a maximum flow rate up to about 800 liters per minute.

87. The apparatus of claim 86 characterized in that the differential pressure transducer is selected from among one of a venturi section having a first and second cross sectional areas and a flow resistive screen, and the converting means is characterized by means for converting the differential pressure measured across the transducer into a flow rate using an array of predetermined calibration constants.

88. The apparatus of claim 86 characterized in that the inspiratory flow path further comprises means for providing a laminar air flow across the differential pressure transducer.

89. The apparatus of claim 88 characterized in that the differential pressure transducer and the laminar air flow means further comprise at least three flow resistive screens interposed in series across the air flow path characterized in that the differential pressure is measured across the middle screen.

90. The apparatus of claim 81 further characterized by means for enabling the device for delivering aerosolized medications when it is sufficiently agitated and disabling the device from delivering aerosolized medication when it is not sufficiently agitated.

91. The apparatus of claim 83 further characterized by a filter disposed in the inspiratory flow path for minimizing contamination of the flow transducer.

92. The apparatus of claim 81 characterized in that the supply of aerosol generating material is in open communication with the aerosol flow path proximate to the supply when the supply is seated in the receptacle.

93. The apparatus of claim 85 characterized in that the tube and nozzle are disposable components of the device.

94. The apparatus of claim 81 further characterized by a visual display device for providing a measure of the supply of aerosol seated in the receptacle.

95. The apparatus of claim 82 further characterized by a microprocessor and memory for recording a log history of the aerosol delivered and the sensed inspiratory flow of each valve actuation including the date, time and amount of aerosol delivered.

96. An apparatus for inhalation therapy of a patient characterized by:

a sensor for monitoring a patient's breath flow including inspiratory flow through a flow path;

an inhaler device containing a supply of aerosol generating material including medication for releasing an amount of aerosol medication for inspiration in response to a detected inspiratory flow exceeding a delivery threshold;

means for determining a pulmonary function based on a measure of the detected breath flow;

means for comparing a first determined pulmonary function based on a first detected breath flow and a second determined pulmonary function based on a second detected breath flow and determining relative changes in pulmonary function in response to released aerosol medication over time.

97. The apparatus of claim 96 further characterized by means for adjusting the amount of aerosol medication released from the reservoir in response to the determined

relative change in the first and second determined pulmonary functions.

98. The apparatus of claim 96 further characterized by a display device for indicating whether the patient's pulmonary function is improving, degrading or remaining nominally the same.

99. The apparatus of claim 98 characterized in that the display device includes a first visual display for indicating an improving pulmonary function and a second visual display for indicating a degrading pulmonary function.

100. The apparatus of claim 96 further characterized by signal generator for indicating a desired breath flow pattern for determining the pulmonary function to be determined.

101. The apparatus of claim 97 characterized in that the inhaler device determines a delivery threshold in response to a first detected inspiratory flow and releases the adjusted amount of aerosol medication in response to a following detected inspiratory flow satisfying the determined delivery threshold.

102. The apparatus of claim 101 characterized in that the determined pulmonary function is adjusted based on the patient's predetermined health characteristics.

103. The apparatus of claim 97 characterized in that the inhaler device determines whether a first detected inspiratory flow satisfies a preselected delivery threshold and releases the adjusted amount of aerosol in response to the first detected inspiratory flow satisfying the preselected delivery threshold; and is further characterized by means for lowering the preselected delivery threshold in response to the first detected inspiratory flow not satisfying the preselected delivery threshold and the inhaler device releases the adjusted amount of aerosol medication if a subsequently detected inspiratory flow satisfies the lowered delivery threshold.

104. The apparatus of claim 103 characterized in that the inhaler device recursively lowers the lowered delivery threshold a predetermined amount in response to the last detected inspiratory flow not satisfying the previous lowered delivery threshold.

105. The apparatus of claim 104 characterized in that the determined pulmonary function is adjusted based on the patient's predetermined health characteristics.

106. A method for controlling inhalation therapy using an inhaler device including a supply of aerosol generating material including medication and having a valve for releasing an amount of aerosolized medication for inspiration by a patient in response to a sufficient inspiratory flow characterized by:

monitoring a patient's breath flow including the inspiratory flow;

determining a pulmonary function based on a detected breath flow;

comparing a first determined pulmonary function based on a first detected breath flow and a second determined pulmonary function based on a second detected breath flow; and

determining relative changes in the determined pulmonary function in response to aerosol medication released over time.

107. The method of claim 106 further characterized by adjusting the amount of medication to be released from the supply by the inhaler device in response to the determined relative change in the first and second pulmonary functions.

108. The method of claim 106 further characterized by displaying an indication of whether the determined pulmonary function is improving, degrading, or remaining nominally the same.

109. The method of claim 108 characterized in that an improving condition is displayed on a first visual display and a degrading condition is displayed on a second visual display.

110. The method of claim 106 further characterized by generating a signal for indicating a desired breath flow pattern for determining the pulmonary function to be determined.

111. The method of claim 106 characterized in that identifying a sufficient inspiratory flow for the release of an amount of aerosol medication is characterized by selecting a delivery schedule based on a first detected inspiratory flow and releasing the amount of aerosol when the following detected inspiratory flow satisfies the selected delivery schedule.

112. The method of claim 111 further characterized by adjusting the determined pulmonary function based on the patient's predetermined health characteristics.

113. The method of claim 106 characterized in that releasing the amount of aerosol medication is characterized by:

comparing a first detected inspiratory flow to a preselected delivery threshold;

releasing the amount of aerosol medication in accordance with the delivery schedule in response to the detected inspiratory flow satisfying the delivery threshold;

lowering the preselected delivery schedule in response to the detected inspiratory flow not satisfying the preselected delivery threshold;

comparing a subsequently detected inspiratory flow to the lowered delivery threshold and;

releasing the amount of aerosol medication in accordance with the lowered delivery schedule in response to the subsequently detected inspiratory flow satisfying the lowered delivery threshold.

114. The method of claim 113 further characterized by recursively lowering the lowered delivery schedule a predetermined amount in response to the last detected inspiratory flow not satisfying the previous lowered delivery threshold.

115. The method of claim 114 further characterized by adjusting the determined pulmonary function based on the patient's predetermined health characteristics.

116. Apparatus for displaying a measured pulmonary function of a person characterized by:

a flow path;

a sensor for monitoring a breath flow of the person through the flow path;

means for determining a pulmonary function of the person based on a measure of the sensed breath flow;

a first visual indicator corresponding to a first predetermined range of pulmonary functions;

a second visual indicator corresponding to a second predetermined range of pulmonary functions; and

means (2000) for illuminating the visual indicator whose preselected range includes the determined pulmonary function.

117. The apparatus of claim 116 further characterized by a signal generator for indicating a desired breath flow pattern for determining the pulmonary function to be determined.

118. The apparatus of claim 116 further characterized by a third visual indicator corresponding to a third predetermined range of pulmonary functions, characterized in that the first, second, and third visual indicators respectively indicate predetermined ranges of acceptable pulmonary functions, marginal pulmonary functions, and unacceptable pulmonary functions.

119. The apparatus of claim 116 characterized in that the sensor detects the expiratory flow rate and the determined pulmonary function is FEV1.

120. The apparatus of claim 118 further characterized by:

means for comparing a first determined pulmonary function based on a first breath flow and a second determined pulmonary function based on a second breath flow and determining whether or not the person's determined pulmonary function has changed over time; and

means for indicating that the determined pulmonary function has improved on the first visual indicator, nominally remained the same on the second visual indicator, and degenerated on the third visual indicator in response to the determined change in the determined pulmonary function.

121. The apparatus of claim 116 further characterized by:

a canister of aerosol generating material;

a valve for releasing an amount of aerosol generating material from the canister to form an aerosol; and

means for operating the valve to deliver a selected amount of aerosol in response to the determined pulmonary function and a detected inspiratory flow occurring subsequent to the sensed breath flow so that the selected amount of aerosol is delivered for inspiration by the person during the detected inspiratory flow.

122. The apparatus of claim 116 further comprising:

means for comparing a first determined pulmonary function based on a first breath flow and a second determined pulmonary function based on a second breath flow and determining whether or not the person's determined pulmonary function has changed from the first to the second determinations;

a supply of aerosol generating material;

a valve for releasing an amount of aerosol generating material from the supply to form an aerosol; and

means for operating the valve to release a selected amount of aerosol in response to the first and second determined pulmonary functions and a detected inspiratory flow occurring subsequent to the first and second breath flows characterized in that the selected amount of aerosol is adjusted in response to the determined change in pulmonary function and released for inspiration by the person during the detected inspiratory flow.

123. A method for displaying a measured pulmonary function of a person characterized by:

monitoring the breath flow of a person through a flow path;

measuring a breath parameter of the detected breath flow;

determining a pulmonary function of the person based on the measured breath parameter;

illuminating a first visual indicator in response to the determined pulmonary function being in a first range of pulmonary functions; and

illuminating a second visual indicator in response to the determined pulmonary function being in a second range of pulmonary functions.

124. The method of claim 123 further characterized by generating a signal indicating a desired breath flow pattern for measuring the breath parameter used for determining the pulmonary function to be determined.

125. The method of claim 123 further characterized by illuminating a third visual indicator in response to the determined pulmonary function being in a third range of pulmonary functions, characterized in that the first, second, and third visual indicators correspond respectively to selected ranges of acceptable, marginal and unacceptable pulmonary functions.

126. The method of claim 123 characterized in that determining the pulmonary function is characterized by determining the FEV1 based on measuring the expiratory flow rate.

127. The method of claim 125 further characterized by:

comparing a first determined pulmonary function based on a first breath flow to a second determined pulmonary function based on a second breath flow;

determining whether or not the person's determined pulmonary function has changed from the first to the second determinations; and

indicating that the determined pulmonary function has improved on the first visual indicator, remained nominally the same on the second visual indicator, and

degenerated on the third visual indicator in response to the determined change in pulmonary function.

128. The method of claim 123 further characterized by:

selecting an amount of aerosol to be released from a canister of aerosol generating material in response to the determined pulmonary function;

detecting an inspiratory flow subsequent to the detected breath flow; and

releasing the selected amount of aerosol for inspiration by the person during the detected inspiratory flow.

129. The method of claim 123 further characterized by:

comparing a first determined pulmonary function based on a first breath flow to a second determined pulmonary function based on a second breath flow;

determining whether or not the person's determined pulmonary function has changed from the first to the second determinations;

selecting an amount of aerosol to be released from a supply of aerosol generating material in response to the first and second determined pulmonary functions and any determined change in pulmonary function;

detecting an inspiratory flow subsequent to the first and second detected breath flows; and

releasing the selected amount of aerosol for inspiration by the person during the detected inspiratory flow.

130. A hand held device for administering aerosolized medication for inhalation therapy of a patient characterized by:

a sensor for monitoring breath flow through a flow path;

a clock for providing the date and time;

an inhaler device for releasing a selected amount of aerosol from a supply in response to a sensed inspiratory flow satisfying a delivery schedule; and

a recorder for recording sensed breath flow data and the date and time the breath flow data was sensed.

131. The apparatus of claim 130 characterized in that the recorder records a log of the date, time and amount of each amount of aerosol released during any sensed inspiratory flow.

132. The apparatus of claim 131 characterized in that the recorded log includes the magnitude of the sensed inspiratory flow at the time of release of each amount of aerosol.

133. The apparatus of claim 130 further characterized by means for determining a pulmonary function of the person based on a detected breath flow, characterized in that the recorder records a log of the time, date, determined pulmonary function and detected breath flow data for each determined pulmonary function.

134. The apparatus of claims 132 and 133 characterized in that the recorder is characterized by a microprocessor and memory, further characterized by a data port for transmitting the recorded log data to an external device.

135. The apparatus of claim 132 further characterized by a display device for indicating a measure of the amount of aerosol remaining in the inhaler device supply.

136. The apparatus of claim 131 further characterized by means for evaluating the recorded log and inhibiting the inhaler device from releasing medication if such release would result in an overdose of medication.

137. The apparatus of claim 133 further characterized by a display device for displaying the determined pulmonary function.

138. The apparatus of claim 133 characterized by a display device for displaying relative changes over time of the determined pulmonary function.

139. A method for administering aerosolized medication for inhalation therapy using an inhaler device for releasing an amount of aerosol from a supply into a sensed inspiratory flow, characterized by:

monitoring breath flow through a flow path;

monitoring the operation of a clock providing date and time information;

releasing a selected amount of aerosol in response to a detected inspiratory flow satisfying a delivery threshold; and

recording a log of the date, time and amount of aerosol released each time an amount of aerosol is released.

140. The method of claim 139 characterized in that recording the log is further characterized by recording the magnitude of the inspiratory flow at the time of each release of an amount of aerosol.

141. The method of claim 140 further characterized by:

determining a pulmonary function of the detected breath flow; and

recording in the log the time, date, determined pulmonary function and determined breath flow data for each determined pulmonary function.

142. The method of claim 139 further characterized by displaying a measure of the amount of aerosol remaining in the supply.

143. The method of claim 139 further characterized by evaluating the recorded log data over a selected recent time interval and inhibiting the release of an amount of aerosol if such release would result in an overdose of the medication.

144. The method of claim 141 further characterized by displaying the determined pulmonary function.

145. The method of claim 141 further characterized by displaying relative changes in the determined pulmonary function over time.

146. The method of claim 139, 140 or 141 characterized in that the log is recorded in the memory of a microprocessing system associated with the inhaler device, and is further characterized by transferring the contents of the recorded log to an external device.

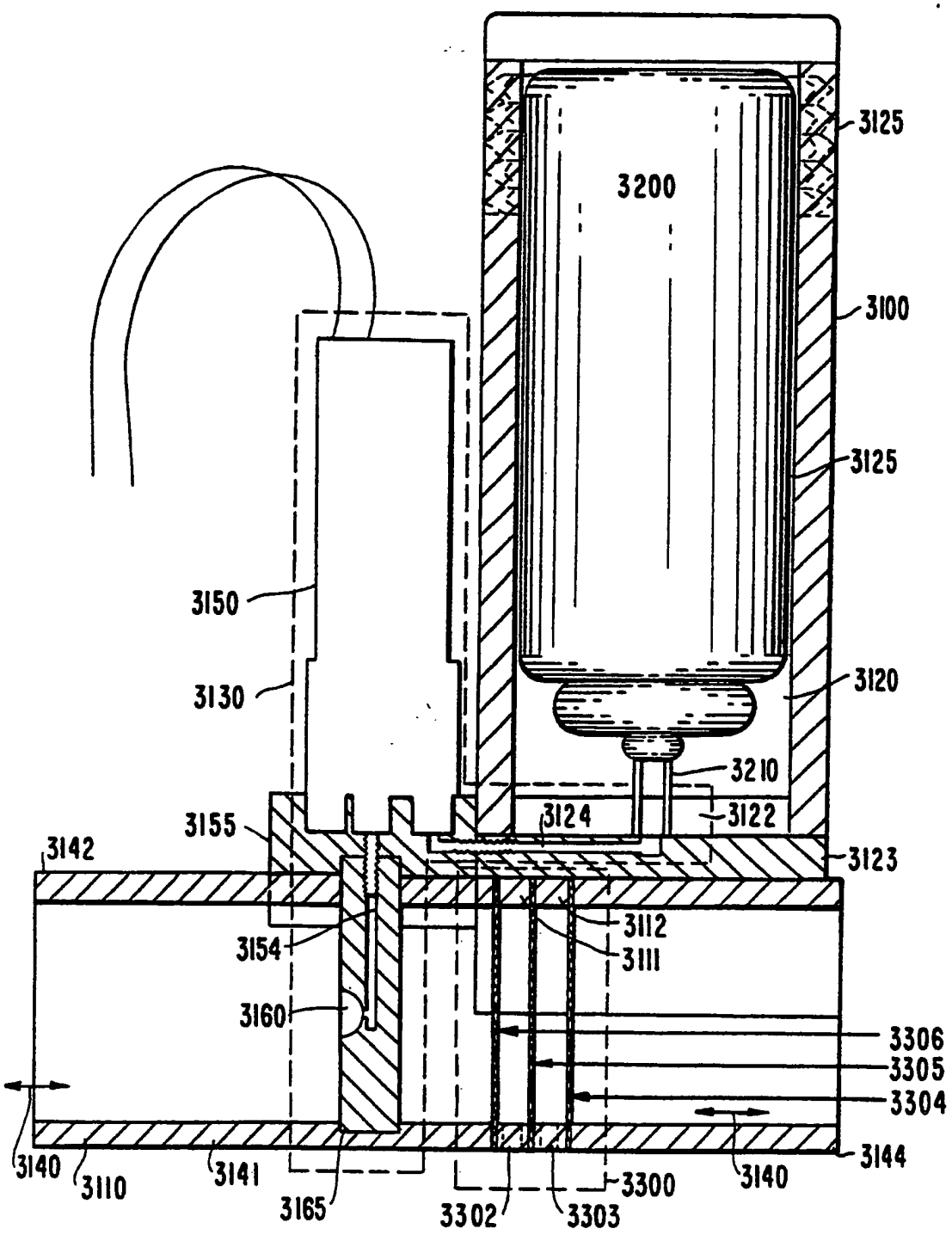

3125
3200
3100
3125
3150
3130
3120
3210
3155
3124
3122
3142
3123
3112
3154
3111
3160
3306
3305
3304
3140
3110
3141
3165
3302
3303
3300
3140
3144

FIG. 1

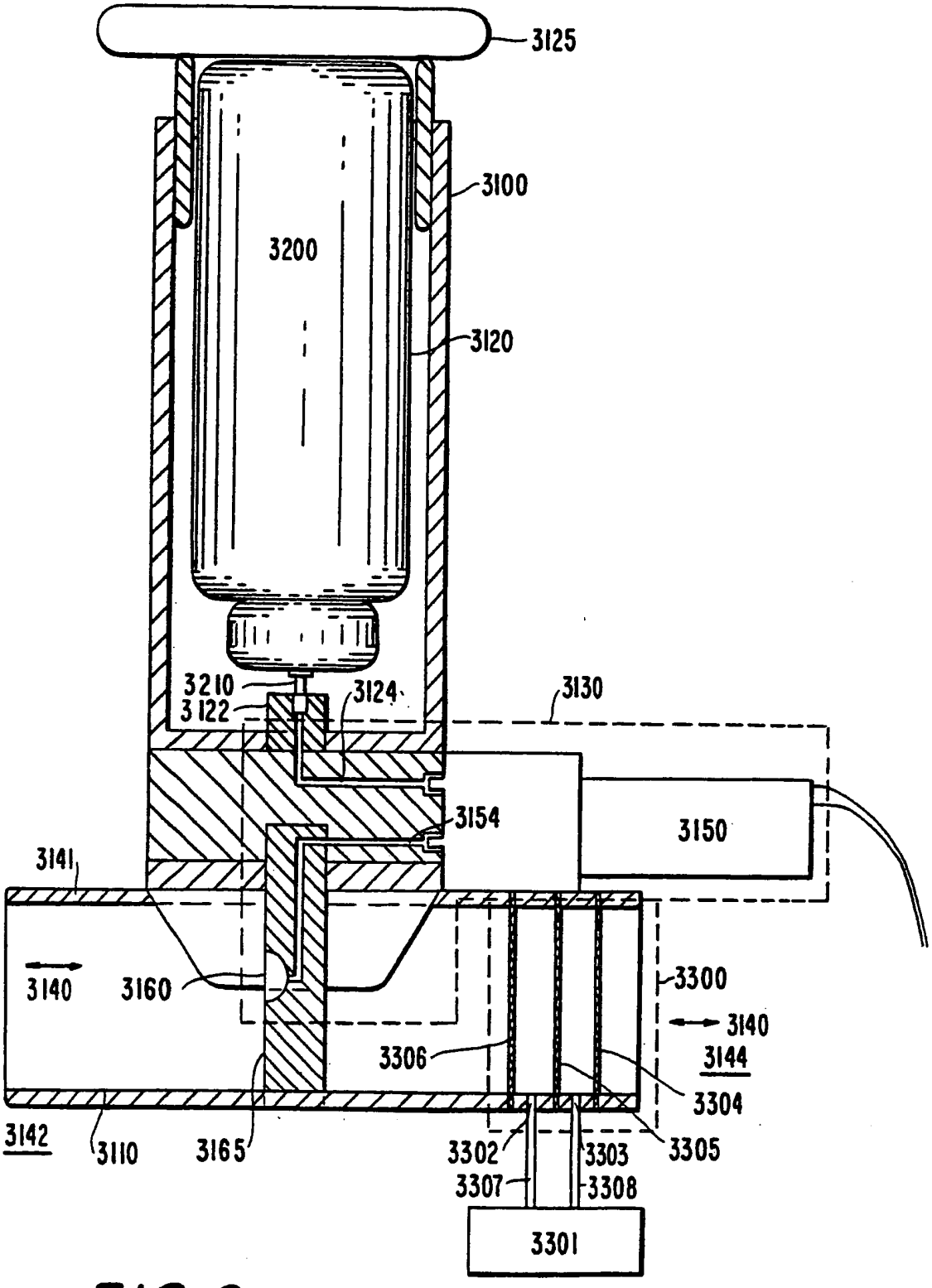

3125
3100
3200
3120
3210
3122
3124
3130
3154
3150
3141
3140
3160
3300
3140
3144
3306
3304
3142
3110
3165
3302
3303
3305
3307
3308
3301

FIG. 2

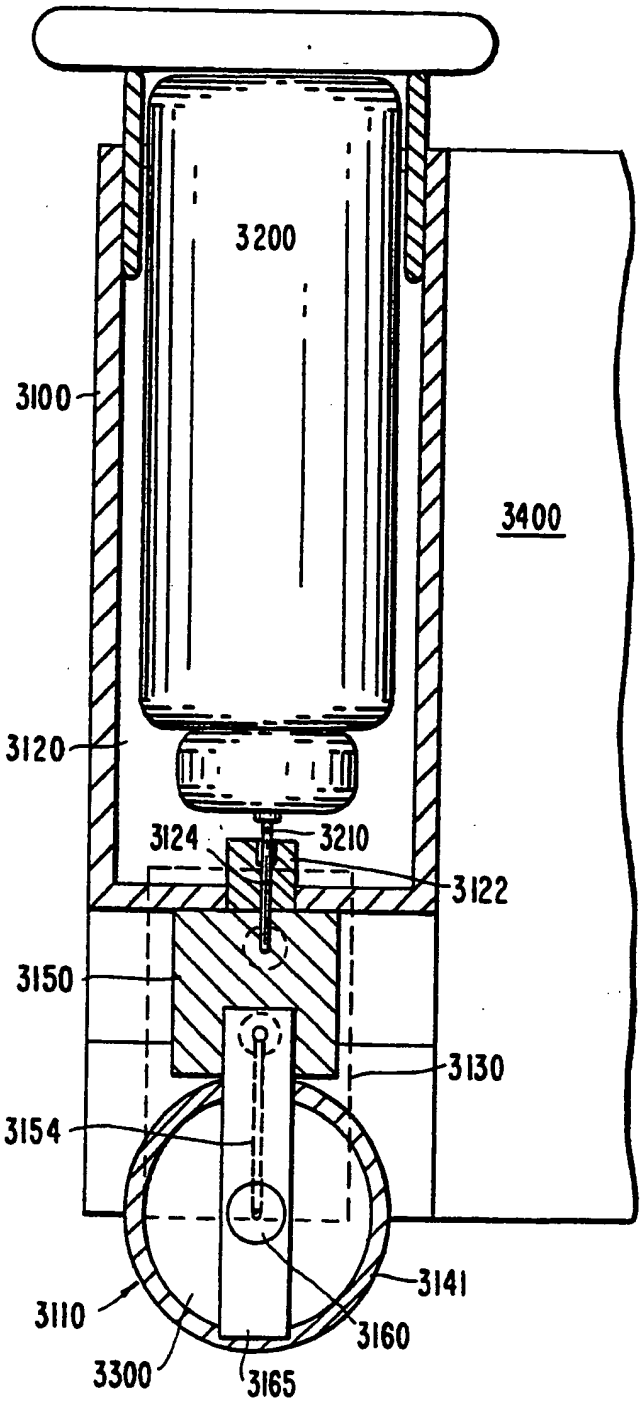
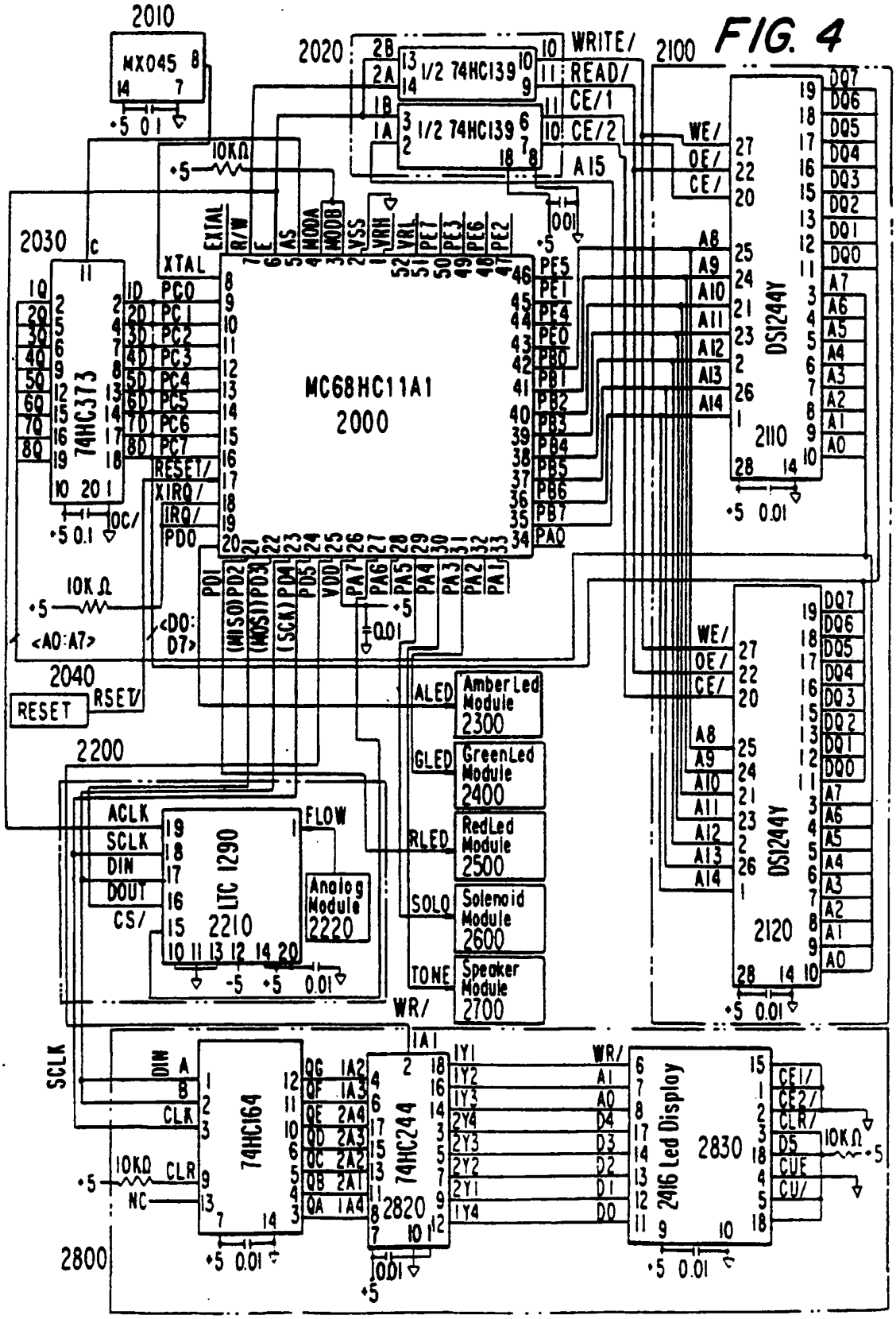

3200
3100
3400
3120
3124
3210
3122
3150
3130
3154
3141
3110
3160
3300
3165

FIG. 3

FIG. 4


2010
MX045
2020
1/2 74HC139
WRITE/
READ/
CE/1
CE/2
A15
2100
WE/
OE/
CE/
DSI244Y
2110
2120
2030
74HC373
MC68HC11A1
2000
XTAL
EXTAL
R/W
E
AS
MODA
MODB
VSS
VRH
VRL
PE7
PE3
PE6
PE2
PC0
PC1
PC2
PC3
PC4
PC5
PC6
PC7
RESET/
XIRQ/
IRQ/
PD0
PD1
PD2
PD3
PD4
PD5
VDD
PA7
PA6
PA5
PA4
PA3
PA2
PA1
PE5
PE1
PE4
PE0
PB0
PB1
PB2
PB3
PB4
PB5
PB6
PB7
PA0
10KΩ
<A0:A7>
<D0:D7>
2040
RESET
RSET/
2200
LTC 1290
2210
ACLK
SCLK
DIN
DOUT
CS/
FLOW
Analog Module 2220
ALED
Amber Led Module 2300
GLED
Green Led Module 2400
RLED
Red Led Module 2500
SOLO
Solenoid Module 2600
TONE
Speaker Module 2700
WR/
2800
74HC164
74HC244
2820
2416 Led Display
2830
CLR
NC
CE1/
CE2/
CLR/
D5
CUE
CU/

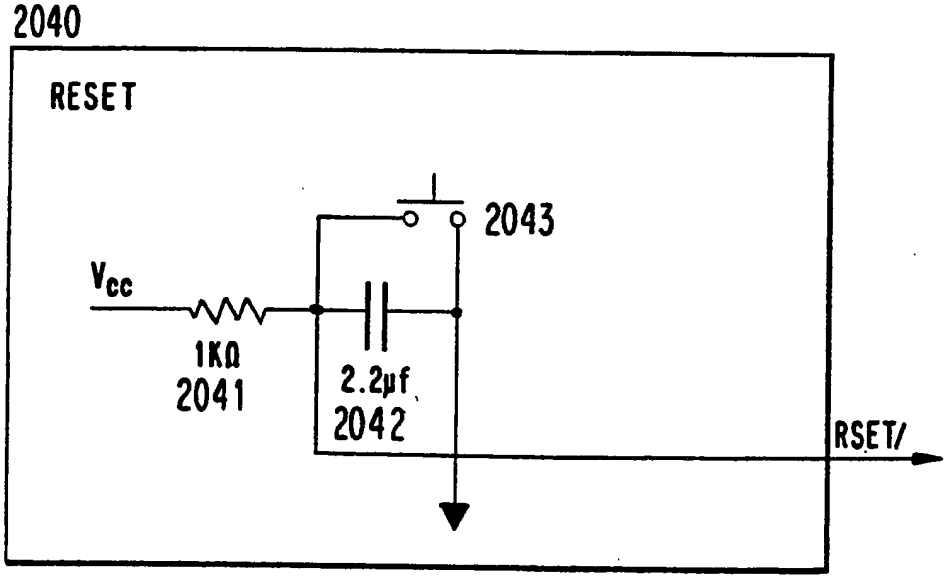
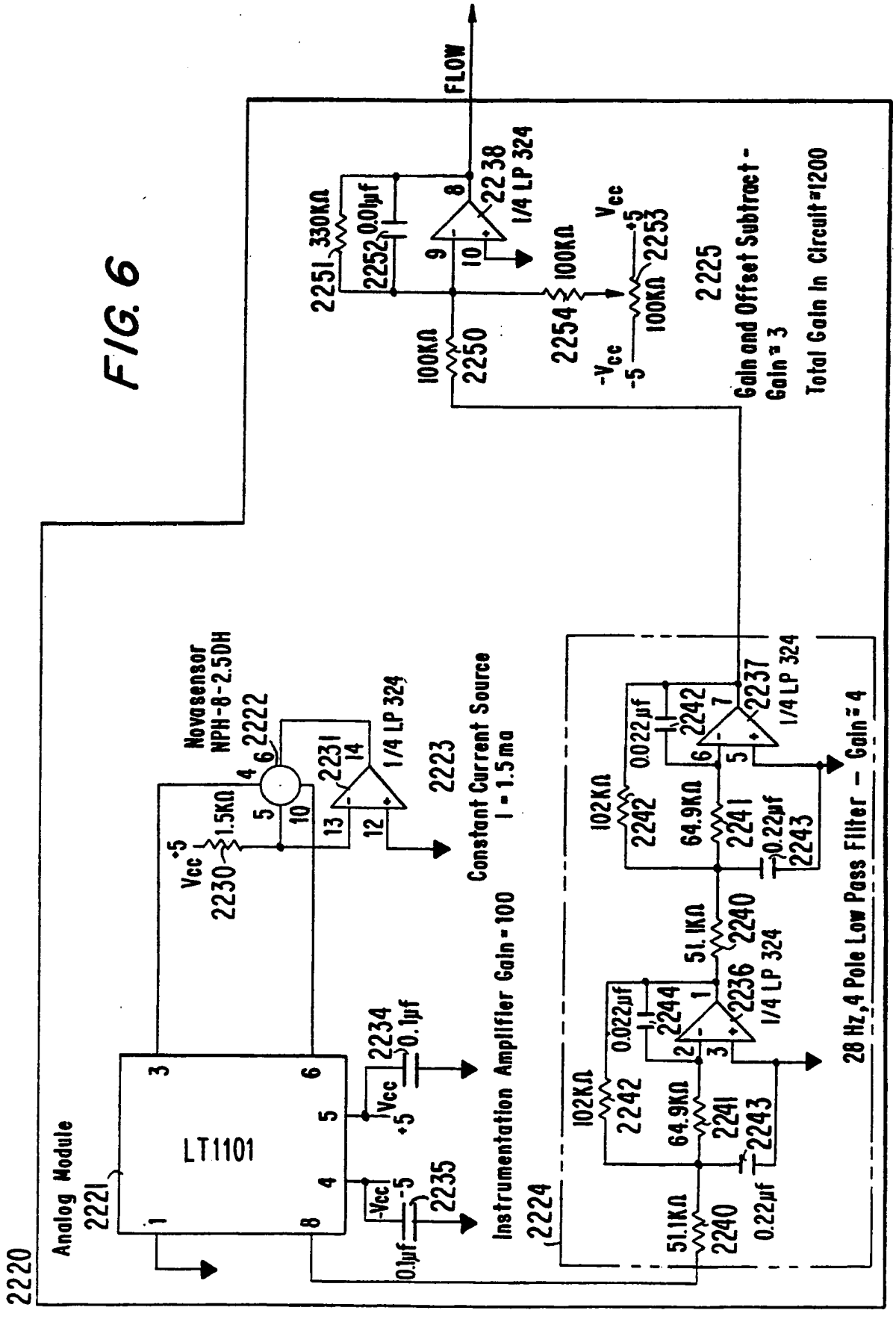


FIG. 5

FIG. 6


2220
Analog Module
2221
LT1101
2234
0.1µf
2235
Instrumentation Amplifier Gain=100
2224
Novasensor
NPH-8-2.5DH
2222
1.5KΩ
2230
2231
1/4 LP 324
2223
Constant Current Source
I = 1.5ma
102KΩ
2242
0.022µf
64.9KΩ
2241
0.22µf
2243
51.1KΩ
2240
2236
2244
2237
28 Hz, 4 Pole Low Pass Filter — Gain=4
2251
330KΩ
2252
0.0µf
2238
100KΩ
2250
2254
2253
2225
Gain and Offset Subtract - Gain=3
Total Gain In Circuit=1200
FLOW

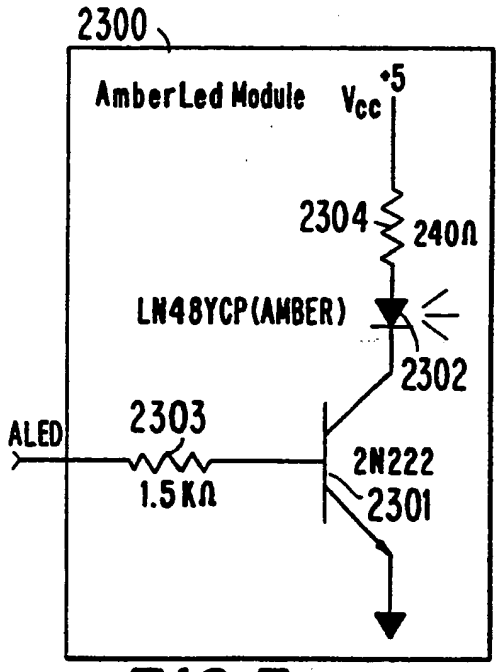


FIG. 7

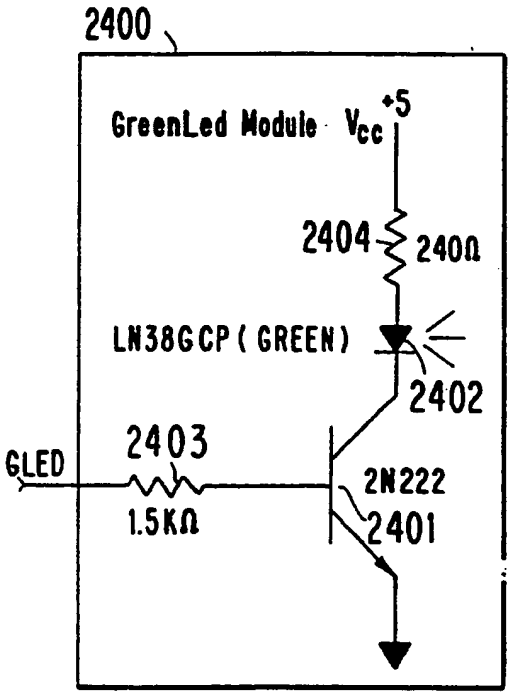


FIG. 8

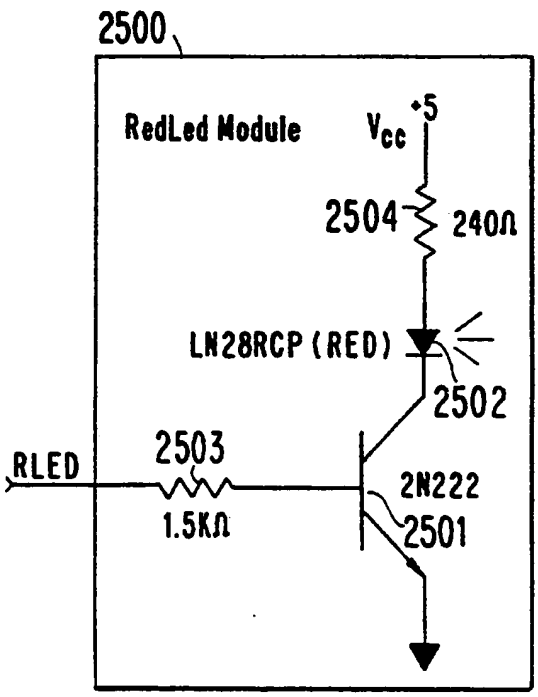


FIG. 9

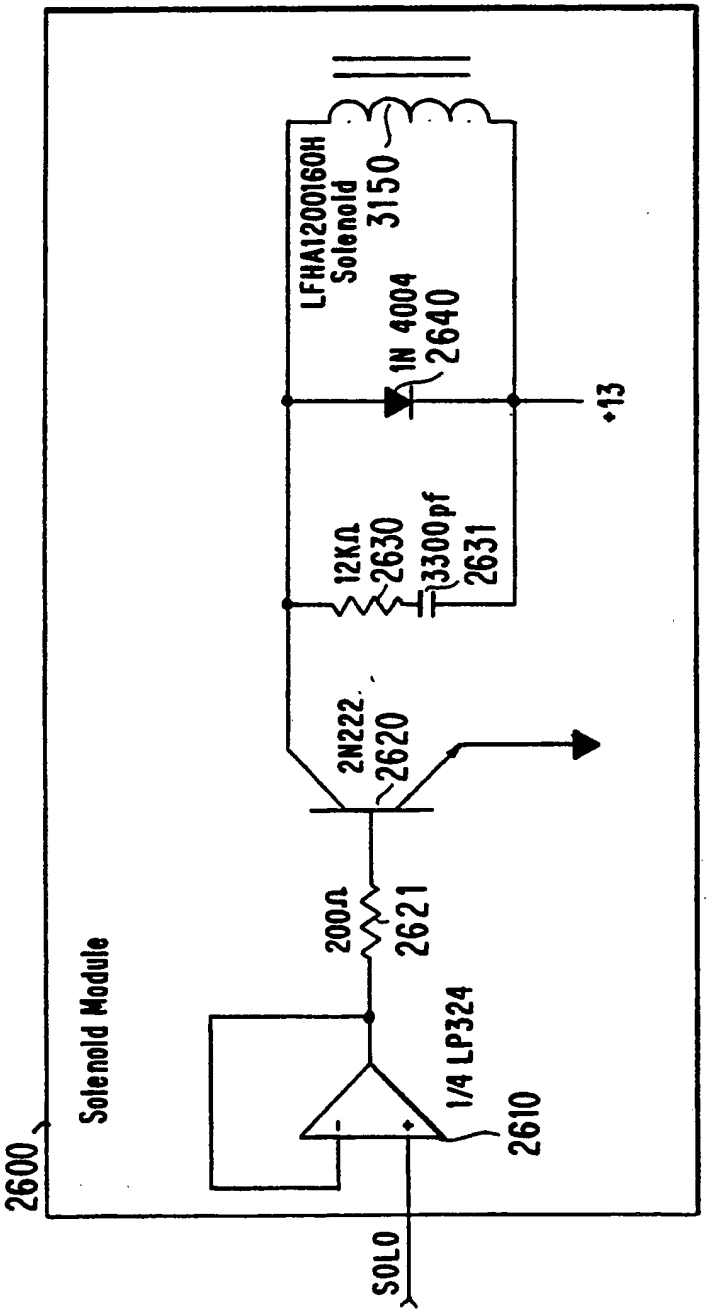

2600
Solenoid Module
SOLO
1/4 LP324
2610
200Ω
2621
2N222
2620
12KΩ
2630
3300pf
2631
1N 4004
2640
LFHA1200160H
Solenoid
3150
+13

FIG. 10

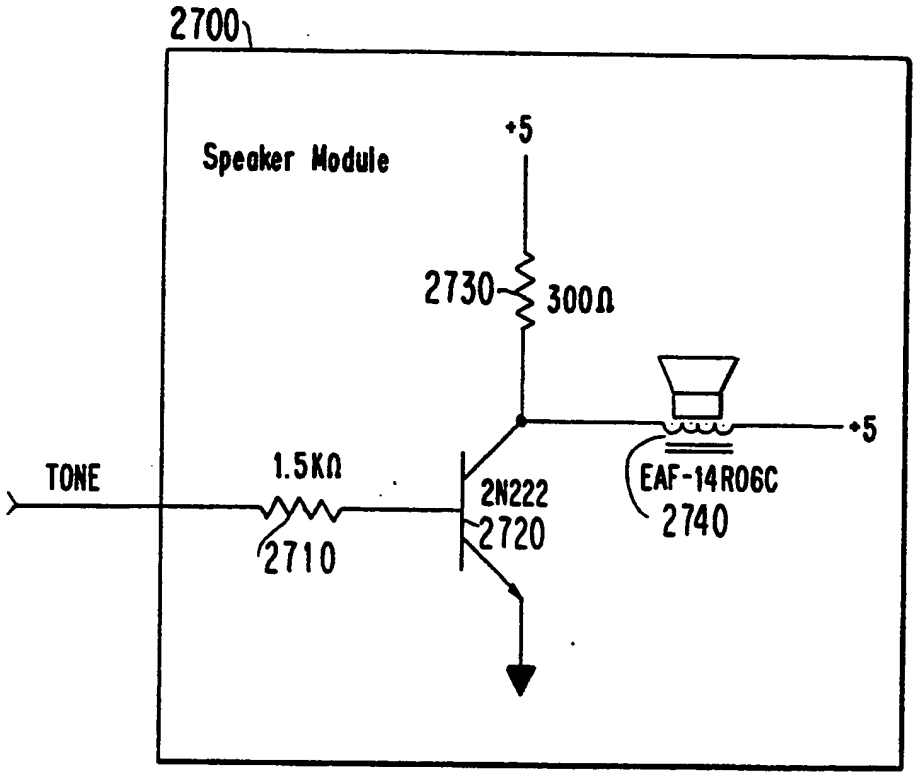

2700
Speaker Module
+5
2730
300Ω
+5
TONE
1.5KΩ
2710
2N222
2720
EAF-14R06C
2740

FIG. 11

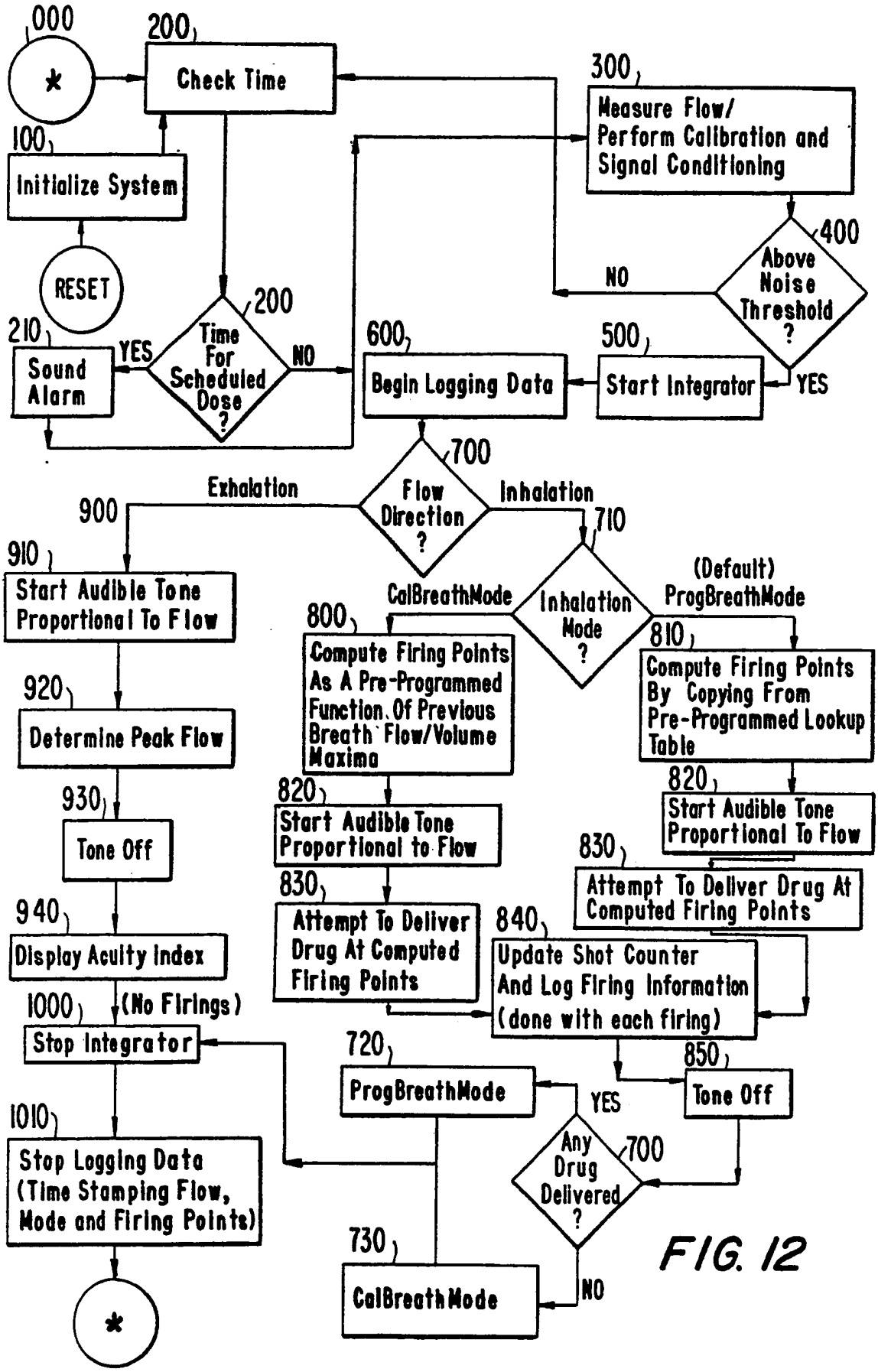

000
*
200
Check Time
300
Measure Flow/ Perform Calibration and Signal Conditioning
100
Initialize System
RESET
400
Above Noise Threshold ?
NO
YES
200
Time For Scheduled Dose ?
NO
YES
210
Sound Alarm
600
Begin Logging Data
500
Start Integrator
700
Flow Direction ?
Exhalation
Inhalation
900
910
Start Audible Tone Proportional To Flow
710
Inhalation Mode ?
CalBreathMode
(Default) ProgBreathMode
800
Compute Firing Points As A Pre-Programmed Function Of Previous Breath Flow/Volume Maxima
810
Compute Firing Points By Copying From Pre-Programmed Lookup Table
920
Determine Peak Flow
820
Start Audible Tone Proportional to Flow
820
Start Audible Tone Proportional To Flow
930
Tone Off
830
Attempt To Deliver Drug At Computed Firing Points
830
Attempt To Deliver Drug At Computed Firing Points
940
Display Acuity Index
840
Update Shot Counter And Log Firing Information (done with each firing)
1000
(No Firings)
Stop Integrator
720
ProgBreathMode
850
Tone Off
YES
1010
Stop Logging Data (Time Stamping Flow, Mode and Firing Points)
Any Drug Delivered ?
700
730
CalBreathMode
NO
*

FIG. 12

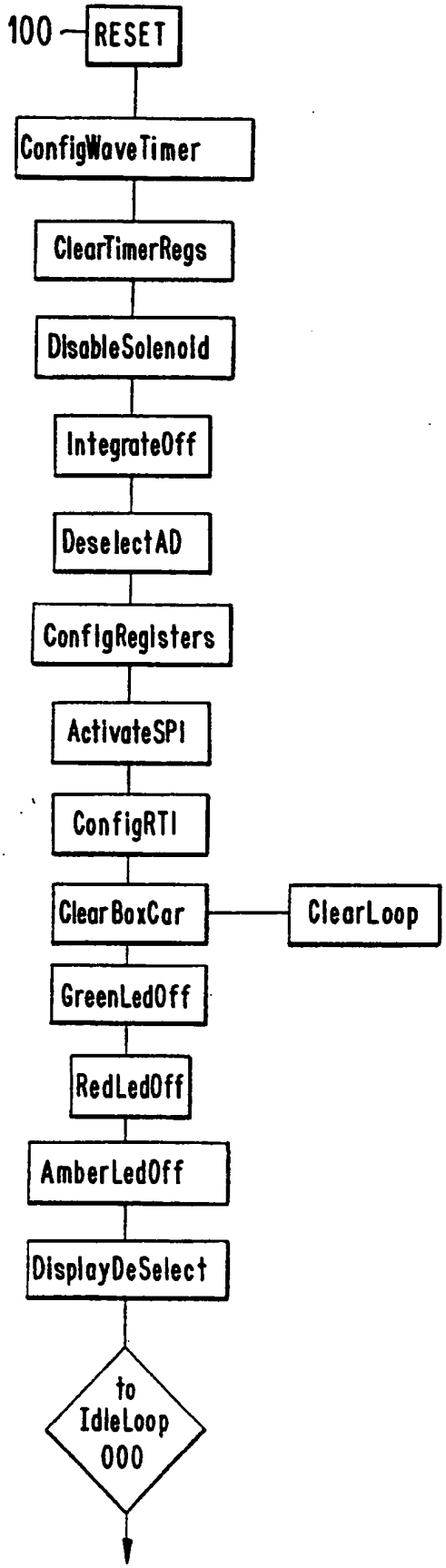

100
RESET
ConfigWaveTimer
ClearTimerRegs
DisableSolenoid
IntegrateOff
DeselectAD
ConfigRegisters
ActivateSPI
ConfigRTI
ClearBoxCar
ClearLoop
GreenLedOff
RedLedOff
AmberLedOff
DisplayDeSelect
to IdleLoop 000

FIG. 13A

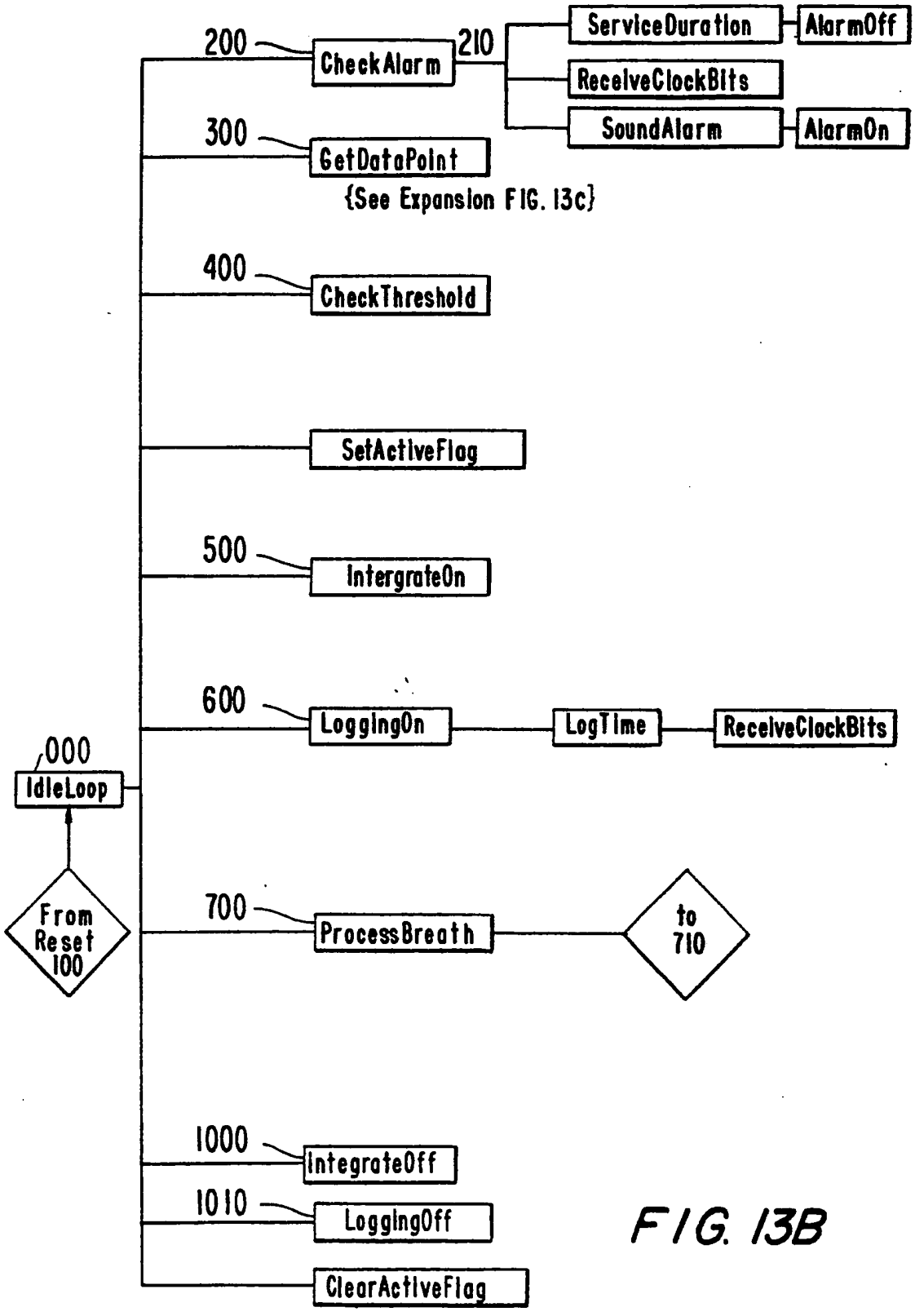

200
CheckAlarm
210
ServiceDuration
AlarmOff
ReceiveClockBits
SoundAlarm
AlarmOn
300
GetDataPoint
{See Expansion FIG. 13c}
400
CheckThreshold
SetActiveFlag
500
IntergrateOn
600
LoggingOn
LogTime
ReceiveClockBits
000
IdleLoop
From Reset 100
700
ProcessBreath
to 710
1000
IntegrateOff
1010
LoggingOff
ClearActiveFlag

FIG. 13B

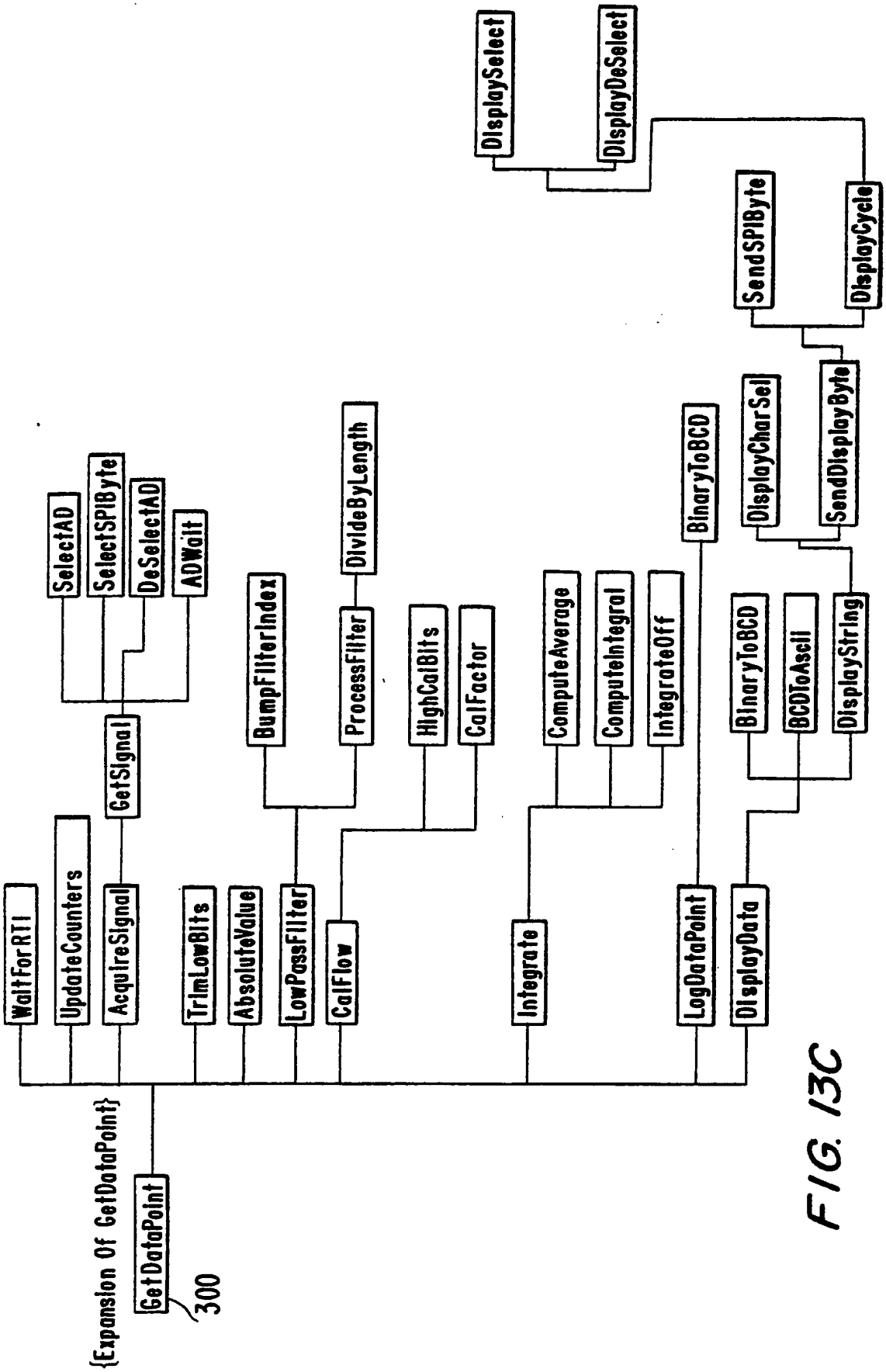

{Expansion Of GetDataPoint}
GetDataPoint
300
WaitForRTI
UpdateCounters
AcquireSignal
TrimLowBits
AbsoluteValue
LowPassFilter
CalFlow
Integrate
LogDataPoint
DisplayData
GetSignal
SelectAD
SelectSPIByte
DeSelectAD
ADWait
BumpFilterIndex
ProcessFilter
DivideByLength
HighCalBits
CalFactor
ComputeAverage
ComputeIntegral
IntegrateOff
BinaryToBCD
BinaryToBCD
BCDToAscii
DisplayString
DisplayCharSel
SendDisplayByte
SendSPIByte
DisplayCycle
DisplaySelect
DisplayDeSelect

FIG. 13C

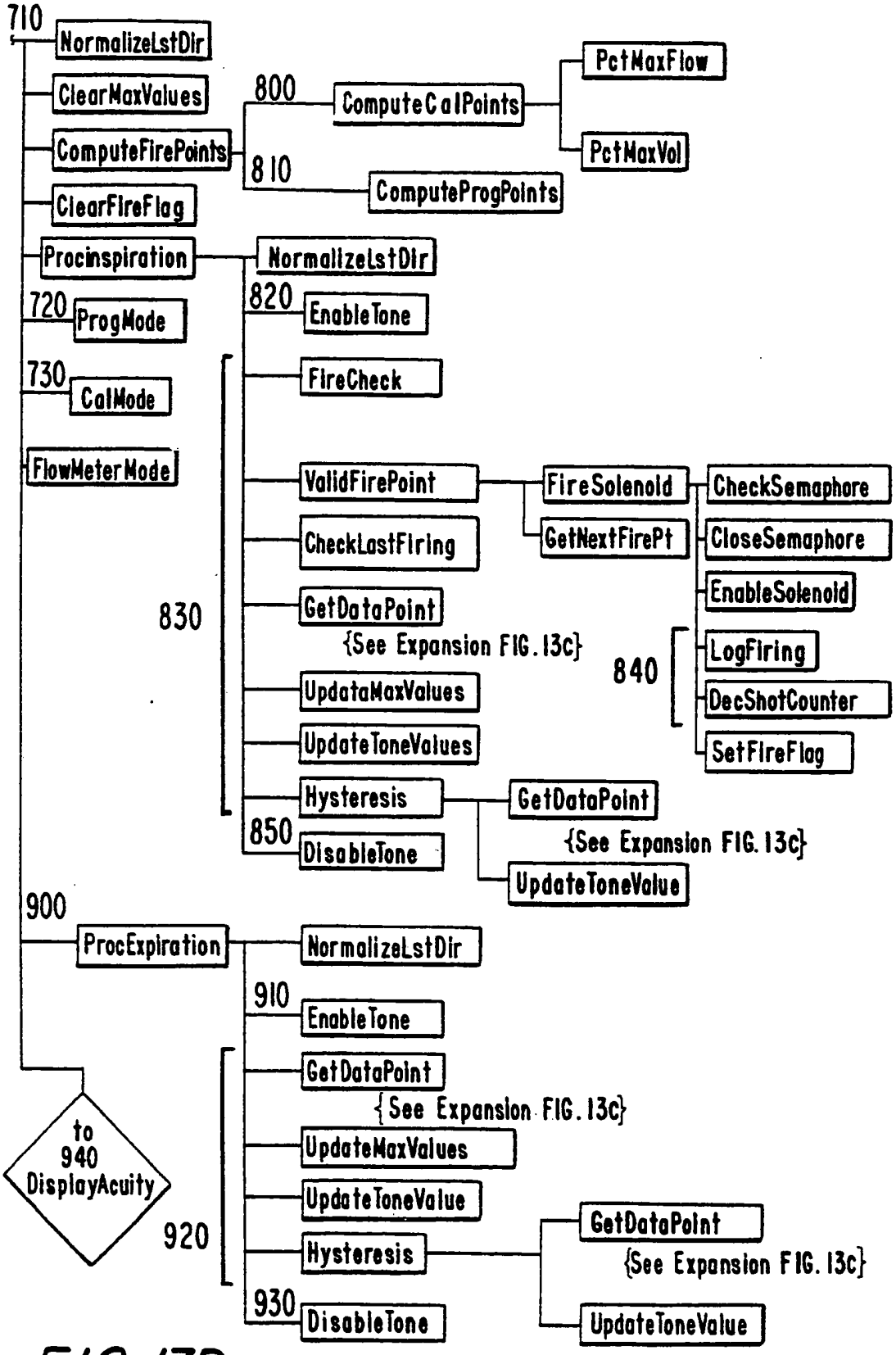

710
NormalizeLstDir
ClearMaxValues
ComputeFirePoints
800
ComputeCalPoints
PctMaxFlow
PctMaxVol
810
ComputeProgPoints
ClearFireFlag
ProcInspiration
NormalizeLstDir
820
EnableTone
FireCheck
720
ProgMode
730
CalMode
FlowMeterMode
ValidFirePoint
FireSolenoid
CheckSemaphore
GetNextFirePt
CloseSemaphore
EnableSolenoid
CheckLastFiring
830
GetDataPoint
{See Expansion FIG. 13c}
840
LogFiring
DecShotCounter
SetFireFlag
UpdataMaxValues
UpdateToneValues
Hysteresis
GetDataPoint
{See Expansion FIG. 13c}
850
DisableTone
UpdateToneValue
900
ProcExpiration
NormalizeLstDir
910
EnableTone
GetDataPoint
{See Expansion FIG. 13c}
to 940 DisplayAcuity
UpdateMaxValues
UpdateToneValue
920
Hysteresis
GetDataPoint
{See Expansion FIG. 13c}
930
DisableTone
UpdateToneValue

FIG. 13D

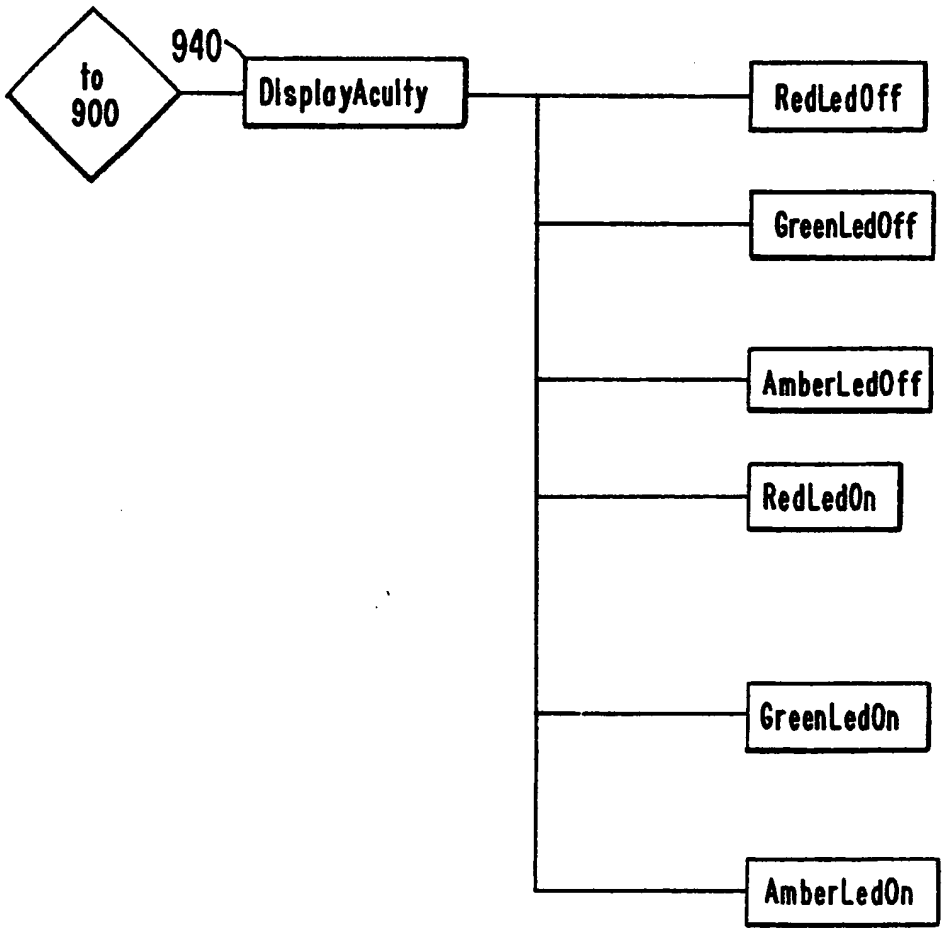

940
to 900
DisplayAcuity
RedLedOff
GreenLedOff
AmberLedOff
RedLedOn
GreenLedOn
AmberLedOn

FIG. 13E

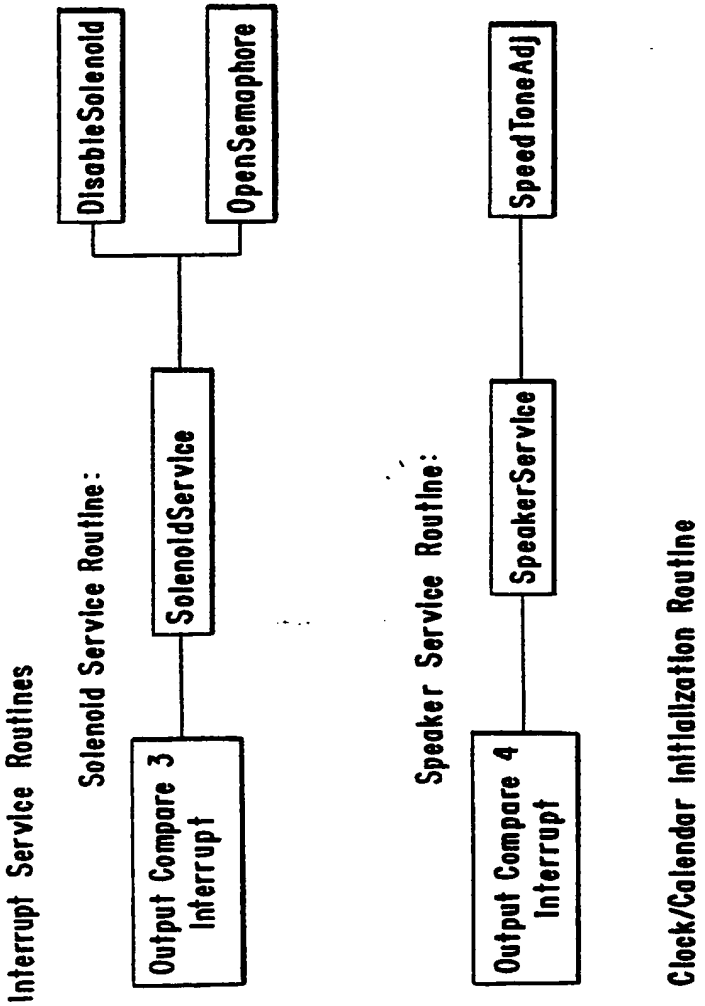

Interrupt Service Routines
Solenoid Service Routine:
Output Compare 3 Interrupt
SolenoidService
DisableSolenoid
OpenSemaphore
Speaker Service Routine:
Output Compare 4 Interrupt
SpeakerService
SpeedToneAdj
Clock/Calendar Initialization Routine
SetClock

FIG. 13F